# INTERNATIONAL CLINICS

## A QUARTERLY

OF

ILLUSTRATED CLINICAL LECTURES AND
ESPECIALLY PREPARED ORIGINAL ARTICLES

ON

TREATMENT, MEDICINE, SURGERY, NEUROLOGY, PEDIATRICS, OBSTETRICS, GYNECOLOGY, ORTHOPÆDICS, PATHOLOGY, DERMATOLOGY, OPHTHALMOLOGY, OTOLOGY, RHINOLOGY, LARYNGOLOGY, HYGIENE, AND OTHER TOPICS OF INTEREST TO STUDENTS AND PRACTITIONERS

BY LEADING MEMBERS OF THE MEDICAL PROFESSION THROUGHOUT THE WORLD

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# CONTENTS OF VOLUME III

## (SEVENTEENTH SERIES)

### TREATMENT

PAGE

SOME PRACTICAL AND THEORETICAL CONSIDERATIONS CONCERNING DIABETES. By David L. Edsall, M.D..... 1

ON THE TREATMENT OF PNEUMONIA AND ESPECIALLY THE ACTION OF METALLIC FERMENTS IN THIS DISORDER. By Albert Robin, M.D..... 25

MECHANOTHERAPY. By John W. Wainright, M.D..... 38

CURABILITY OF TUBERCULOSIS. By E. S. Bullock, M.D..... 50

### MEDICINE

THE BLOOD PRESSURE IN TUBERCULOSIS. By W. B. Stanton, M.D. ..... 60

TWO CASES OF PRIMARY CARCINOMA OF THE LIVER: ONE WITH FIBRINOUS PNEUMONIA; ONE DIAGNOSTICATED BY PARACENTESIS ABDOMINIS. By William Henry Porter, M.D..... 75

ACUTE GASTRITIS. By David Somerville, B.A., M.D., M.R.C.P..... 89

THE SALIENT FACTORS IN THE ESTIMATION OF RENAL DISEASE. By Raymond Wallace, M.S., M.D..... 96

GENERAL ABDOMINAL ENLARGEMENT, WITH SPECIAL REFERENCE TO THE HEPATIC CIRRHOSIS. By Mark A. Brown, M.D... 104

### SURGERY

INOCULABILITY OF TUMORS AND THE ENDEMIC OCCURRENCE OF CANCER. By Leo Loeb, M.D..... 114

SURGERY OF THE BLOOD VESSELS. By J. E. Sweet, A.M., M.D..... 131

INFLAMMATION OF THE GALLBLADDER AND GALL DUCTS. By George Tully Vaughan, M.D..... 149

PAGE

PERFORATING ULCER OF THE FOOT, ITS ÆTIOLOGY AND TREATMENT. By Arthur J. Hall, M.D. ..... 159

SOME SURGICAL ASPECTS OF TUBERCULOSIS. By John B. Roberts, M.D. ..... 162

## GYNECOLOGY

COLLARGOL IN PUERPERAL INFECTION. By E. Bownaire, M.D... 170

ATOPOMENORRHŒA. By F. K. Green, M.D. and Q. W. Hunter, M.D. 179

## GENITO-URINARY DISEASES

CONSERVATIVE PERINEAL PROSTATECTOMY FOR CHRONIC PROSTATITIS. By Hugh H. Young, M.D. ..... 191

THE ETIOLOGY AND EXPERIMENTAL STUDY OF SYPHILIS. By Frederick P. Gay, M.D. ..... 199

SPERMATIC INSUFFICIENCY AND DIASTEMATIC INSUFFICIENCY. By MM. Ancel and Bouin ..... 211

## OPHTHALMOLOGY

A CONTRIBUTION TO THE STUDY OF OCULAR BIRTH INJURY. By Ernest Thomson, M.A., M.D., and Leslie Buchanan, M.D. ..... 217

EXTRACTION OF CATARACT IN THE CAPSULE. By J. Rutter Williamson, M.D. ..... 234

HOW TO TURN BACK THE UPPER EYELID. By Raymond Beal, M.D. 246

## NEUROLOGY

SOME CASES OF POLYNEURITIS (INCLUDING NEUROMYOSITIS) APPARENTLY NOT DUE TO ALCOHOL, ARSENIC OR ANY OF THE ORDINARILY RECOGNIZED CAUSES. By F. Parkes Weber, M.D., F.R.C.P. ..... 253

## DERMATOLOGY

PRESENT TREATMENT OF HYPERTRICHOSIS. By L. Brocq, M.D... 262

## PATHOLOGY

THE RELATION OF INTRACORPUSCULAR CONJUGATION IN THE MALARIAL PLASMODIA TO LATENT AND RECURRENT INFECTIONS. By Charles F. Craig, M.D. ..... 273

# LIST OF ILLUSTRATIONS TO VOLUME III

## (SEVENTEENTH SERIES)

## PLATES


PAGE

Interpapillary adeno-carcinoma (Fig. 2) ..... 78
Extension of carcinomatous growth to ora serata (Fig. 3) ..... 78
Carcinomatous invasion of optic nerve and retina (Fig. 4) ..... 79
Liver with primary and secondary carcinomatous deposits (Fig. 6) ..... 82
Cystic sarcoma of the thyroid of a white rat—original tumor (Fig. 1) .. 121
Cystic sarcoma of the white rat, transplanted tumor (Fig. 2) ..... 121
Cyste sarcoma of the thyroid of a white rat (Fig. 3) ..... 121
Papillary adenocarcinoma of a white mouse (Fig. 4) ..... 121
Adenocarcinoma of a white mouse, in all probability originating from the mammary gland (Fig. 5) ..... 121
Lymphosarcoma of dog (Fig. 6) ..... 121
Mouse with multiple carcinomata (Fig. 7) ..... 121
Original carcinoma in Japanese mouse (Fig. 8) ..... 124
Carcinoma of the Japanese mouse (Fig. 9) ..... 124
Spindle cell sarcoma found in the II generation inoculated with carcinoma of Japanese mouse (Fig. 10) ..... 124
Epithelium growing into Agar (Fig. 11) ..... 130
Growth of epithelium of a guinea pig in coagulated blood serum (Fig. 12) ..... 130
Epithelial pearl developing in epithelium in coagulated blood serum (Fig 13) ..... 130
Skin of guinea pig after a series of retransplantations, showing large masses of horn that are formed (Fig. 14) ..... 130
Small transitory tumor in the ovary of a young guinea pig (Fig. 15) ..... 130
Dissection showing enormously distended common bile duct (Fig. 1) ..... 156
Illustration showing perforating ulcers of foot (Fig. 1) ..... 160
Illustration showing perforating ulcers of foot (Fig. 2) ..... 160
Illustration showing perforating ulcers of foot (Fig. 3) ..... 160
Illustration showing perforating ulcers of foot (Fig. 4) ..... 161
Section from human chancre stained by the Levadite Method, showing the spirochæta pallida (Fig. 1) ..... 204
Diagram of the posterior surface of the cornea of Case A, which shows blood on the posterior elastic lamina (Fig. 1) ..... 233
Meridional section of the cornea of Case A magnified 15 diameters, showing rupture of the posterior surface of the cornea (Fig. 3) ..... 233
Meridional section of the left cornea of Case F, magnified 18 diameters, showing rupture of the posterior surface of the cornea (Fig. 3) ..... 233

PAGE

Appearance of the posterior surface of the cornea in Case E, high power, showing the separation of the posterior elastic lamina, with massing of pigment (Fig. 4) ..... 233
Drawing of the right cornea of Case J, showing a faint haze in the neighborhood of the linear opacities (Fig. 5) ..... 233
Drawing of the left cornea of Case K (Fig. 6) ..... 233
Drawing of the linear opacities and adjacent haze in the right cornea of Case B (Fig. 7) ..... 233
Photograph to illustrate method of controlling eyelids (Fig. 1) ..... 240

## FIGURES

Primary carcinoma of the liver (Fig. 1) ..... 77
Temperature chart ..... 80
Chart showing outline of liver (Fig. 1) ..... 106
Chart showing the positions of linear opacities in ten cases observed clinically (Fig. 8) ..... 222
Illustration to show method of turning back the eyelid (Fig. 1) ..... 247
Illustration to show method of turning back the eyelid (Fig. 2) ..... 248
Illustration to show method of turning back the eyelid (Fig. 3) ..... 249
Illustration to show method of turning back the eyelid (Fig. 4) ..... 249
Illustration to show method of turning back the eyelid (Fig. 5) ..... 250
Illustration to show method of turning back the eyelid (Fig. 6) ..... 251
Illustration to show method of turning back the eyelid (Fig. 7) ..... 251

# Treatment

## SOME PRACTICAL AND THEORETICAL CONSIDERATIONS CONCERNING DIETETICS*

BY DAVID L. EDSALL, M.D.

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I HAVE been generous to myself in my title, but I have no intention of attempting to race through the whole field that is open to me, for I shall find myself sufficiently busy in trying, in the time that I may properly use, to outline the views that I have gradually formed regarding a few guiding points in dietetics. These views are, in most particulars, not very different from those of many other persons; but they involve matters that are fruitful subjects for thought and discussion.

I do not think that I differed very much from most other persons in the same circumstances in having had, when I graduated in medicine and for a long time afterwards, a most confused and hopeless feeling of ignorant empiricism in my attempts to diet patients. I believe I do no violence to facts in stating that in almost all medical schools the subject of dietetics is treated in a very casual way, though I think we are all agreed that there is no more important division of the whole subject of therapeutics. Fragments regarding dietetics, both scientific and practical, are, to be sure, taught nearly everywhere; but they are ordinarily fragments; and very frequently the scientific principles are taught by a physiologist separately, and essentially as a part of a pure science; while the practical portion is acquired from other sources, and, as a rule, merely in the form of isolated facts regarding the treatment of special diseases—the facts being usually not given in very great

* An Address delivered before the Clinical Society of Washington, D. C., March 16, 1907.

detail, and being presented to the student in such a form that he does not gain guiding principles, but simply remembers that in this disease he is to give certain foods or certain culinary preparations, and in other diseases other forms of diet. The scientific side of the question usually appears to be chiefly so much more burden to be carried for his examinations, and nearly always seems to him of little practical interest and value. He commonly does not see how he can join it fast to the actual treatment of the sick, calories and similar terms sound like so much unintelligible jargon, and he soon dismisses them from his mind. Little of the known constitution of foods is taught him, except a few figures about their nutritive value and the like; and these ordinarily seem of small moment to him from a practical standpoint.

When he comes to the actual prescribing of diets for patients, he has, if I may use myself as an example, only isolated instances in which there are illuminating facts to follow; such instances, for example, as the unsuitability of starches in diabetes. Usually he tells nearly everyone, with a stricken sense that the patient knew this before, that fried things and many sweets or pastries are indigestible; he gathers in a few more routine regulations to insist upon; and he occasionally grows bold enough to suspect that a particularly well-fed looking patient eats too much, or that another who points with the usual pride to a gouty family-history ought to cut down his meats or do something else—he is not quite sure which. In most cases that he meets, however, in arranging other details he merely accepts the statement of some authority that a certain diet or certain articles of food are unsuitable; or he follows the lead that the patient so often gives one, as to personal peculiarities. He comes to decide things by means of his own judgment only after he has had considerable empirical experience, or has gone through the still more difficult process of bringing some order out of the chaos of his own mind by devoting special thought and study, and perhaps some detailed investigation, to the subject.

In my more recent experience as a teacher, I have often found that if one asks a student, who is about to graduate, to write out the exact details of the diet that he would order for an individual case of almost any disease, he is likely to be wholly at sea, and he is ordinarily still more confused, if one desires a reasonable explana-

tion of the many regulations that he suggests. Matters are not very different with many of us after we have been for some years licensed to practise; and I think that most experienced doctors, when arranging a diet-list, do it chiefly as the result of their own or some other individual's empirical experience. The results in the latter instances are good or bad, according to the degree of experience and the acuity of judgment of the practitioner; but before anyone acquires experience and reasonable judgment in such matters, he usually goes through a haphazard formative process that is difficult for him and disadvantageous for himself and his patients.

Dietetics is, in many of its details, difficult enough, at best; but it has seemed to me that it would help the student, both before and after his graduation, if, instead of having scientific and practical details given him separately, and the latter chiefly as details, without much regard for the principles on which they are based, it were made the first consideration of the clinical teacher to instruct the student as briefly and concisely as possible how far he can or cannot apply the knowledge gained through scientific research as a guide in actual practice; and likewise to point out certain other general principles that are based partly upon general medical knowledge and partly upon common-sense, experience and acquaintance with humankind. I do not lay claim to superior skill in dieting patients; but my own uncertainties have been largely lessened, and the probability of successful results greatly increased as compared with my earlier efforts, by having formulated some such principles for myself. These principles are, of course, derived in large part from the work of others, and have been made simply by sifting down such work to suit my own views of practical exigencies. In small part they are the consequence of personal work and observation. Given such principles, to start upon, one has the means of judging rationally, in a large proportion of instances, as to the general line of action to be adopted; and the suitability of details in any particular case is then much more readily determined, and one's judgment in detail will depend much less upon hazardous guesses than upon a definite knowledge of the constitution of foods and of food-articles, together with a careful study of the personal and pathological peculiarities of the individual to be cared for.

Our knowledge of both human pathology and the scientific

principles of dietetics is, of course, in many particulars unhappily obscure. Our practices must, therefore, be still largely empirical; and with individuals, they must often be simply tentative. In many cases we meet with dietetic points that cannot be settled wholly rationally; but there is certainly an advantage in using rational knowledge as far as we can, rather than proceeding almost entirely upon empirical lines. The differenc is much the same as sailing with or without a compass.

I shall attempt to describe the manner in which I endeavor in any individual case to formulate my general plan of regulating the diet. I have surveyed what I have written, and I may confess at once that most of it seems elementary and commonplace to the point of triteness. I can only hope that some of you are still behind me in the journey through some parts of the dietetic purgatory and that for such I may be able to make the pathway a little smoother. I shall discuss some of the points that I shall touch upon in a little detail as I mention them. I shall, however, be obliged to eliminate discussion of most details of dietetics, because of the impossibility of covering such matters within a reasonable time. I shall speak more particularly of the measures to be adopted with walking patients or, at least, with those that do not palpably require very severe and peculiar restrictions in their diet; for if an absolutely liquid diet, a diabetic diet, or some such special regulation is required, the indications, as a rule, are comparatively definite and, in such cases, one needs chiefly to acquire knowledge of a considerable menu that he can order, whereas he has relatively little difficulty in determining which sorts of food-articles should be permitted. The more troublesome cases are those in which one must search out the indication for all regulations in each individual instance, those cases in which specific regulations are not furnished by the very name or the severity of the disease, but must be decided according to the special circumstances; such cases, for example, as most instances of digestive disorder and a large proportion of the mild or moderately severe instances of disease of the liver, kidneys, and circulatory organs, as well as those numerous examples of obscure disorder of nutrition that are sometimes due to undernutrition sometimes to general overfeeding or to gourmandizing in particular ways.

The first point to be settled with such patients is whether they need their food-habits altered at all, or whether their trouble appears to be not in any way dependent upon diet; and this is a question that should be decided with practically every patient who has anything of consequence wrong. If the diet needs altering, one must decide, first of all, whether the food should be increased, decreased, or merely altered in character. This point is often exceedingly difficult to settle; for, consciously or unconsciously, many persons tell more untruths about their food than about their morals. They slur over many details, in order to avoid deprivation, or because they dislike to confess their frailties; and they honestly forget many things.

Careful, detailed questioning as to the habits of diet is, of course, a great help in gaining this knowledge; but I continuously have less faith in the reliability of this apparently sensible measure. The best means of learning the food-habits of an individual, if this can be done, is to have him write out, for at least several days, the kind and quantity of food that he has eaten; the general manner of its preparation; the amounts of water, tea, coffee, alcoholic and other beverages taken at meals or between meals; and the amount of tobacco used. Patients do not mind the bother of this, as a rule, for they see the accuracy of the measure; and I think that most persons, when they have to subscribe to a written statement, overlook, either purposely or accidentally, very few things. This record should be obtained, of course, without having previously suggested any changes in the diet. One is then in a position to judge whether the total quantity is proper, whether the relative amounts of the various foods are suitable, whether the manner of preparation is simple or indigestibly complex, and various further minutiæ that are always likely to be overlooked or passed over casually. One can in this manner save much time, as contrasted with asking detailed and searching questions, and waiting for doubtful and hesitating replies.

Let me illustrate the value of such a simple custom in bringing to light facts that otherwise are at times very difficult to learn:—I recently saw a boy of eleven years, who was a little under weight, nervous, and not in satisfactory general condition, but who had no evident cause for his lack of health, except that he always awoke

at about five o'clock in the morning, and stayed awake after that time. The occasion of this could not be elicited until I learned from his records that he had the rather odd habit of drinking three or four glasses of water, or even more, before going to bed. Upon questioning him, I then found that he was always awakened by the necessity for urination. After accomplishing this, he simply felt wakeful, thus losing the two hours or more of subsequent sleep that he should have had. Eliminating the water-drinking at bed-time sufficed to prevent his early waking; he slept until the proper time, and soon got back to pretty satisfactory general vigor.

Having determined what a patient is doing, the next point is to decide whether the amounts and kinds of food and drink reported are proper. We have two chief ways of doing this. One is to determine what the effect of his diet has been upon his weight—whether this is stationary, increasing, or decreasing. One also determines whether the weight is normal, as compared with his general frame; and in regulating his diet, one then increases or decreases in accordance with his previous and subsequent weight-records, and in accordance with the usual habits of humanity. Having told him what kinds of food he can take, one selects the amount of each kind chiefly in accordance with common sense and custom; but one permits much of the regulation to depend upon his appetite for what is allowed him. The subsequent effects are again determined by means of the scales.

This does very well in the great majority of cases, for most persons will take sufficient quantities of what they are permitted to use to prevent their emaciating. The weight-records must, of course, not be accepted too literally as indications; because, for example, before pushing the work of the digestive organs harder by increasing the food, one needs, of course, to determine whether the loss of weight is not due to some cause of overstrain or some discoverable disease that is destroying tissue. One needs, also, to determine carefully, not only that the total amount of food appears to be correct, but likewise whether there is or is not some peculiarity in the kind of food the patient has been choosing that will explain his condition.

I scarcely need to insist upon the necessity for determining that overstrain and tissue-destroying disease are absent, but odd habits

of eating are less frequently sought for as causes of emaciation or other disorder. When these habits are particularly bizarre, as is not uncommon with spoiled children and especially with indulged young women, they may be apparent to the family, but they are, even then, frequently not mentioned, and need to be looked for in the record. Not uncommonly, also, they are of such a kind that it would require a little more technical skill than the family possess to recognize the fact that too little food is consumed. I saw recently, for example, a young man whose occupation required much mental and physical activity and demanded generous feeding. He had grown easily tired, and was losing weight. He presented no evidence of disease, and said that he had a good appetite and ate freely; but his record, when somewhat carefully inspected, showed that he took a light breakfast and that, while his lunch and dinner were bulky and made him feel comfortably full, they consisted almost always of thin soup, meat with the fat carefully removed, and large amounts of such vegetables as spinach, cabbage, lettuce, and tubers, with fruit for dessert. I learned that he had for a long time been accustomed to this diet. While it had an odd attractiveness to him, it was curiously limited to foods that, for the most part, have a very low nutritive value. He needed to be taught, not to eat more, but simply what to eat; and he began to gain as soon as this was done.

The use of the scales, then, is the most readily available, and a very valuable help in ascertaining whether a patient is taking a proper amount of food; but one needs to determine that it is not habits or disease that is producing any abnormality of weight, and one cannot by means of the scales determine directly whether it is the quantity or the quality of the food that is at fault. Both quality and quantity may be faulty in relation to the normal, or in relation to some particular disease from which the patient is suffering. It would clearly be very advantageous, if we could, in addition to using the scales, ascertain, after the manner of the physiologist, what each patient should normally be taking as to amount and kind of food. We could by this means tell whether it is diet on the one hand or habits or disease on the other that is at fault; and could also arrange his diet so that he should come as near the proper figures as the circumstances in his particular case would permit. I think that the ordinary physiological teaching as to nutrition leaves the clin-

ician with the feeling that, if he is to be at all accurate in his methods, he must carefully calculate the value of the diet of each patient; and if he does not do this, he might as well be empirical and be done with scientific accuracy. When the clinician attempts to calculate calories, he finds that there is so much difficulty in determining in practice the actual nutritive value of any ordinary diet, that there is such uncertainty regarding the real normal standards that should be adopted, and that there is such a complexity of pathological conditions that must take precedence of physiological rules, that he dismisses about all the teaching of the physiologist as of no practical value.

A middle course is the more successful plan, and is entirely practicable. With the great majority of cases, it is impossible and unnecessary to attempt to calculate the calorific value of the diet. This is an exceedingly difficult matter for the investigator to do accurately. It would require at the least exact records of the weights of each food-article taken daily, and laborious computation of the value of each; and this, particularly with the daily variations in the character of the food and the manner of preparing it, would, in practical routine, be intolerably burdensome and indeed often utterly impossible. I think, therefore, as to our ordinary cases, we must be guided in ordering quantities by our general and decidedly approximate knowledge of the amounts ordinary persons usually take of the foods that we permit them to have. We must then trust chiefly to our own common sense and to the patient's appetite to secure for him the proper total amount, and must depend chiefly upon the record of his weight to determine whether he is doing properly.

But the work of the physiologist is by no means valueless to the clinician. Suppose that the necessities of the case demand a diet wholly different from the normal, as is true in the severe acute diseases or in many cases of diabetes, for example; or suppose, as is often the case with gourmands and the obese, and not infrequently with persons who have various other diseases, that one wishes to restrict somewhat severely the total amount of food taken. If one trusts entirely to empirical methods, one is, in such cases, in danger either of failing to accomplish what one desires or, because one does not know accurately what one is actually giving, of carrying

the restriction so far as to reduce the intake of food to a dangerous degree, without appreciating it until it becomes evident that the diet is harming the patient. One is, indeed, if he uses such a method, pretty certain to do these things occasionally, unless a good deal of experience and at least a moderate amount of conservatism serve to prevent it; particularly if one has not a pretty clear conception of the value of common food-articles. Furthermore, in many cases the appetite may not suffice to lead the patient to take enough; or the choice may be so restricted that he does not himself know how to get enough, even though hungry, unless the way is pointed out to him with some care and with detailed accuracy.

In order to meet such cases properly, I think one should arm one's self with at least an elementary knowledge of the value of ordinary food-articles, in order to have an approximate knowledge of the value of the articles likely to be ordered in such cases; and I believe, too, that the calculated calorific values of a few simple diet-lists of this kind, as found in any work on dietetics, should be noted carefully as guides. Preferably, also, the physician should practice himself in calculating the calorific value of the simpler diets that he is likely to use in such cases. A little practice will enable one to work out with extreme readiness the calorific value of a very simple diet, with the aid of a good table of food-values; and it is not at all difficult with somewhat more complex diet-lists. This calculation of the calorific value of a diet is the worst bug-bear of most men who desire to be accurate in their dietetic methods, particularly in the earlier days of their interest in the matter. It is vastly less difficult in the limited class of cases in which it appears to me to be clinically desirable than it is commonly thought to be.

In order to do it, it is necessary to know only the amount and kind of food being given, to determine from tables what this food contains of protein, fat, and carbohydrate, to multiply by the calorific values and add the products. Indeed, in many tables, such as the valuable tables published by the Department of Agriculture, the calorific value for a given weight of all the common foods is furnished; and one then has merely to reckon the proper value for the amount of food that is given. To calculate the calorific equivalent of any mixed diet is, as I have said, difficult and often impossible; but it takes only a few minutes with a simple diet.

In using liquid diets, for example, when the patient is ordinarily being decidedly restricted in the total value of his food, it makes a great deal of difference whether one simply reckons by quarts or ounces, and has only an indefinite idea of the food-value of a quart or ounce of any particular food; or whether, on the other hand, one knows the exact value of this liquid food as compared with another, and is able thereby to determine exactly what is being done. If one knows, for instance, that two liters of milk, or about two quarts, have a food-value of about 1400 calories, while two liters of an ordinary broth have as a rule a food-value of only about three hundred calories, one appreciates the primary advantage of milk as a fluid diet much more clearly than if one simply knows in a general way that milk is more nutritious than other liquid foods. If it would take about eight or ten quarts of an ordinary broth to maintain a fair-sized adult's nutrition in passably good order during absolute rest in bed, it is manifest that it is not wise to temporize any longer than necessary if some patient is able to take only a quart and a half of broth in twenty-four hours. Again, it often sounds fairly satisfactory to say that a patient is getting, for example, twelve ounces of broth, ten ounces of albumin-water and about two ounces of some patent fluid food-preparation, and this may be all that he can take; but it is much more illuminating, to my mind, to say that he is getting less than three hundred calories, and ought to be getting at least four to five times this amount, if he is to improve, or even hold his own. It surprises most doctors, too, to tell them that the expressed juice of fresh beef, which is often proudly given in teaspoonful-doses, has only one-sixth to one-eighth the nutritive value of milk; that it would take ten to fifteen quarts to furnish a suitable daily ration for a well man, when he is at rest. Beef-juice has a useful place; but, from a nutritional standpoint, its place is usually made altogether too large.

This determination of the calorific value of simple diets is frequently helpful in convalescence from acute disease. I have repeatedly had occasion to do nothing more for a patient who was emaciating dangerously, when he should have been approaching convalescence from an acute disease, than to direct the attention of his medical attendant to some point such as these that I have mentioned. There is a very common tendency, and a very unfortunate

one, to limit the diet in convalescence too greatly. This is done half unconsciously at times as a result of caution.

Occasionally, one can, by determining the value of the diet exactly, clear up the often obscure question whether a patient's nutrition is poor on account of his diet or because of some disorder that is not clearly evident. I was recently seeing, with a skilful pediatrist, an infant convalescent from a severe acute disease, who, for some not very manifest reason, refused to gain; and the question arose as to whether this was due to the fact that we had very considerably reduced the infant's milk-mixture because of slight digestive disturbance, and had gone too far; or whether, on the other hand, there was not some slight disturbance still which might make any increase in the diet likely to damage the child,—a point of importance in this case. A calculation of the calories in his mixture showed 1025. He had previously been gaining well on a diet containing 1060; and it seemed apparent therefore that the diet was not at fault. The mixture was not changed; and, after a week or so, the child began to gain on the same diet. We were both in doubt as to the cause of the trouble in this case; and both had inclined to believe that we ought to push the food a little, until the calories had been calculated. The unexpectedly close approach to the calorific value of the previous diet was explained by a fact that is not easy to consider sufficiently when one habituates himself to mere percentage-figures or total ounces per day in using infants' milk-mixtures; namely, the child was getting one or two more feedings a day than he had previously had, and the extra milk sugar in these feedings practically sufficed to cover the deficiency.

The essential value of the practice may be illustrated by analogy. One would scarcely be satisfied to be told that a patient is getting a teaspoonful of a strychnia-solution or even that he is getting a teaspoonful of a 1:2000 strychnia-solution, if one did not know whether the amount being given contains one-sixtieth or one two hundred and fiftieth of a grain. I feel dissatisfied, when in a tight place, if I do not know whether a patient is getting two hundred or twelve hundred calories.

I should like to insist with some emphasis, both for the sake of accuracy and for the sake of the patient's pocket, upon the importance of knowing exactly what one is doing when one uses

proprietary food-preparations. Manufacturers nearly always praise these products extravagantly and, directly or covertly, they commonly make claims for these preparations utterly beyond their desserts; and I find that a large proportion of medical men accept these claims at their face value, and have a corresponding degree of faith in the foods. If one determines their actual value, one learns, as a rule, that exceedingly little food is being given a patient, when he is taking the amount of these preparations that it is usually possible to administer. For instance, I recently examined chemically a bread-substitute for diabetics and dyspeptics, which is made by a company with a wide reputation. They advertise extravagant statements as to the constitution of this preparation; and these statements I found to come barely within fifty per cent. of the truth,—a somewhat important difference in dietetic matters. Still more rhetorical exclamations are printed regarding its nutritive value. As to the latter, the simple expedient of weighing a specimen-roll showed that, if absolutely all the weight were reckoned as nutritive material, and this is undoubtedly over-generous, one would, in order to get a nutritive value equal to a five-cent loaf of bread, be obliged to use twenty-five to forty of those rolls, and would have to pay a dollar and a half to two dollars for them. As to the common fluid proprietary food-preparations, I know of none that has, ounce for ounce, greater food-value than milk; and most of them, indeed, have a much lower food-value than milk. When one considers the relatively great cost of the proprietary foods and the fact that one can administer in a day, at best, only a few ounces of most of them, while one can use milk even by the quart, I think that their standing as foods becomes more apparent. Their alcohol-content also is usually so high as to make them very unsuitable in many cases.[1]

If we have determined with sufficient accuracy the calorific value of a diet, we must, in order to get our bearings, have a standard with which to compare it; and such standards we must get from the physiologist. There has been an enormous amount of discussion of the correct standards for the two most important points to be

[1] The actual composition of many of the most commonly used liquid proprietary foods has since been made apparent in a most valuable report of the Council on Pharmacy of the American Medical Association. *Jour. Amer. Med. Assoc.*, May 11, 1907.

decided; namely, the total amount of food and the total amount of protein, protein being, of course, absolutely essential in the diet, because our essential tissues are constructed from it. Recently this discussion has been rendered more acute and active, although in this country it has particularly concerned itself with the amount of nitrogenous food. I cannot take time to go into an extensive discussion of my attitude in regard to this matter; but I may say that, while I consider any standard flexible and approximate, and while any that is adopted must be used simply as a guide, and be modified for individuals, whether well or sick, an approximate standard must be adopted as a guide; and I am likewise convinced that the older standards approach much more closely to suitable guides than do the more recent and lower ones. What I have to say regarding this matter represents, in most particulars, equally my views concerning the total food-demand and those concerning the demand for protein.

Certain observations, especially the recent admirable studies of Chittenden, demonstrate that persons can maintain a nutritive balance, and can continue in good health for a considerable length of time, on an amount of food much lower than that which we have been taught is necessary, and on an amount of protein that is certainly not over half the usual amount. We have heard, as the consequence of this experimental work, much insistance upon the doctrine that is often promulgated by both professional men and the laity, that most of humanity eat far too much, and particularly far too much protein. I frankly state that I am entirely out of sympathy with this teaching, in the form in which it is generally put forward and in which it has recently been exploited. I am profoundly convinced that if it were accepted as a law of dietetics, it would do an enormous amount of harm. Indeed, I am sure that faith in this teaching has already damaged individuals who have come under my notice after having practised such methods for some time.

The work that has been done simply demonstrates the minimum amount that a person may take without evident harm. It is, however, illogical and unsafe to accept the minimum as a standard. The standard should, of course, be the most favorable quantity; and the optimum is, in any question, so far as I know, never the minimum, except when we are dealing with things that are essentially

evil, and food is scarcely this. In this point lies what appears to me to be the patent error of this recent teaching. Physiological economy in dietetics does not consist in reducing the labors of the organs engaged in digesting and assimilating food to the lowest point compatible with apparent health and comfort, any more than does physiological economy in exercise consist in using the muscles as little as possible in carrying on one's life; nor does economy in respiration consist in the most infrequent and shallow breathing that we can adopt without evident dyspnœa. Likewise, while excess in protein does cause increased demand upon the organs of metabolism and excretion, we have absolutely no reason for saying that we should reduce the activity of these organs to the lowest point possible. Indeed, most functions do better if they are exercised somewhat; and, so far as the digestive organs, for example, are concerned, it has been clearly shown that their functional secretions, and even their size, are modified directly in proportion to the things that it is necessary for them to do. If this demand is kept very low, one can easily, therefore, reduce their functional capacity to a point much below the normal. Each function that we have is supplied to us in much greater abundance than is requisite for ordinary purposes; and it is evidently desirable that we should have more of everything than the mere minimum amount absolutely essential for the ordinary conditions of life. This appears to me a mere matter of common sense and common finance. We do not, for ordinary purposes, absolutely need all the lung-capacity we have; but for not uncommon extraordinary purposes, we do. I think the presumption is strongly in favor of our needing a higher degree of nutrition than is provided by the minimum, and I believe the evidence shows that we do; for the studies of groups of people whose circumstances require them to reduce their diet to a point closely comparable to Chittenden's recommendations demonstrate that, as groups, their nutrition, their resistance to disease, and their productive capacity are poor.

I insist somewhat warmly upon this point of view, because I have very earnest feelings about the matter. As clinicians, our duty is to see how far theoretical principles can be made to fit actual conditions of life, not to attempt to make the conditions fit those principles that appear to individuals to be correct. As things are,

I believe that the most common error made in prescribing diets is to make the amount too scanty, either unwittingly, because the variety of foods is made so limited that the patient has difficulty in securing a sufficient total quantity; or deliberately, because the idea is followed that persons usually eat too much. A large proportion of the people that I see that have previously been on a diet have either lost vigor, and usually some weight, or have gained neither of these, when they should have done so; while they have improved when the diet was increased. There are undoubtedly many persons who do over-eat, but this is a question that must be settled in each individual case, not by any rule of thumb, and not even by learning the tastes and income of the patient; but by finding out, carefully and in detail, what he actually does as to food. If this is done, I am quite convinced that, of the persons that a doctor sees professionally, at least as many will be found to be suffering from underfeeding as from overfeeding. Hence, the harm of promulgating the doctrine of an overfed humankind.

As to the protein-ration, while this subject is somewhat out of place at this point, I may save time by stating now that what I have just said applies equally to this question. As to my own experience in the matter, I have made estimations of the urinary nitrogen in a great many individuals, and, in ordinary circumstances, this is a direct index of the protein-intake. The large majority of those that habitually took amounts so small as to approach those recommended by Chittenden were in poor health. As further evidence of the harmfulness of attempting to establish a general reduction of the protein-ration, I would say that a considerable proportion of those persons were subjects of those indefinite disorders of nutrition that are usually described under the name "gouty diathesis"; and yet they had grown worse upon the reduced nitrogen-diet, but very frequently improved when the nitrogen-intake was increased to about the ordinary standard. And such persons are just those with whom routine restriction would appear most suitable.

I am not so conservative, however, in my views regarding the variety of foods that a patient takes. An extremely large proportion of the patients that we see, patients with the most varied kinds of medical ills, are suffering largely from the immediate or remote

effects of eating complex and elaborate forms of food. I grant, in one sense, that a large proportion of humanity overeat; but they overeat less in quantity than in quality. If one takes the trouble to estimate approximately the total amount of food taken by persons that deserve to be classed as gourmands, one will, I think, find in a large proportion of instances that the total is not excessive; but if the character of the food, and particularly its manner of preparation, be learned, it will usually be found to be faulty. If the errors in details be corrected, the total amount can ordinarily be very soon, if not at once, brought to the previous level; and, indeed, often judiciously increased.

In spite of what I have said, however, when one comes to the actual choice of the diet, I think that the first rule for persons with most disorders is temporarily, and as a wholly preliminary measure, to reduce the food somewhat, simply for the purpose of giving the patient a partial dietetic rest; not because he has necessarily eaten essentially too much, but because he is out of order and usually cannot successfully do at once what is normal. If he appears to be simply underfed, such a procedure is, of course, out of place; but underfed persons are commonly both underfed and otherwise disordered, and they then temporarily need the same measure. The degree of reduction needs, of course, to be varied according to circumstances. If a typhoid patient, for instance, has decided digestive disturbance, there is urgent indication for restriction; and I practically starve him for a day or two, just as I should practically starve a baby with a digestive upset. I, of course, do this with other persons that have acute gastric or intestinal disturbance; and I believe that with nephritics that are seriously toxic, or with others whose metabolic or excretory processes are overburdened, starvation for from one to several days, providing other circumstances justify this, is an exceedingly valuable measure, in that it helps them to get cleared out through eliminating the necessity for metabolizing and excreting the products of new portions of food.

I always, however, look upon starvation as a very serious measure, and one to be very carefully controlled; and I have absolutely no regard for the modern recrudescence of the doctrine of starvation in disease, a doctrine that leads some enthusiasts to such lengths as ten days or more of water-diet in typhoid fever. Even

when the restriction is but moderate, it is a thing that must be carefully watched, and in most cases continued for only a short time. A great deal of harm is done, I am sure, by continuing a low diet for an indefinite period because the first effects are good. The original symptoms frequently improve; but the general nutrition quickly becomes more or less depraved, and the lowering of the general tone prevents improvement of health and not infrequently makes the patient worse.

There is, I think, too common a tendency to tell patients chiefly what they should not eat. Often in the beginning, and always after one has got the patient well started on a dietetic regime, one should be equally interested in telling him what he should eat; and the latter is often by far the more difficult thing to do skilfully. Therefore, after the preliminary reduction, which is by no means always necessary, one's main effort in this regard should very frequently be directed especially toward improving the patient's general nutrition.

An even more generally applicable rule than the one I have just mentioned, and a rule that may often be held to much longer, is simplicity in the number of food-articles permitted and in the manner of their preparation. The sin that is the cause of the disorder most frequently lies in tickling the palate with elaborate preparations; and the evil effects are due less to excess in amount than to the difficulty that the digestive, metabolic, and excretory organs all have in taking care of the multifarious culinary complexities. I do not think that normal digestion and metabolism are very different from the normal brain in finding a multiplicity of tasks wearing, while an equal burden that is confined to a few things is not. This is still more true of an exhausted brain, and also, I think, of an exhausted or deranged digestion or metabolism. When, therefore, there is any considerable reason for dietetic regulations, I believe that one of the most important sources of success is to start with few food-articles, and to make these of simple character. I feel confident that restriction to a simply prepared diet is even more important than is the actual choice of foods, providing common sense is used in the choice; for we have extremely few dietetic specifics. Judgment must, of course, be exercised in different cases as to the severity of the limitation in choice; but it is practically always wise

to eliminate substances that merely waste labor and provide little or no nutrition, and to eliminate also elaborate mixtures, condiments, sauces, and the like.

The chief difficulty in dietetics with most practitioners is, I think, the result of a struggle to put together a list of food-articles especially suited to the disease at hand owing to the common feeling that diet should have a specific effect in any specific disease. Specific diets for many diseases may be developed in the future; but at present, just as we are obliged to confess that in most diseases we have no specific drugs and, in using drug-therapy, must treat individuals and conditions, rather than diseases; so, in dietetics, we should realize and confess to ourselves that, as a rule, we have no specific principles to follow, and must simply apply our general knowledge of the constitution of foods, not, as a rule, to any special disease; but to a special individual and to the conditions that he presents.

Our choice in the particular kind of foods should depend, first of all, upon the amount of protein, fat, and carbohydrate that we wish to give the patient. It is highly desirable to make our choice of these three food-substances approach in amounts as closely as possible to the quantities taken by the average normal person. The more we learn of the effects of an excess or a lack of any one of these three, the more convinced we must be, I think, that the chief effort in regulating them in dietetics should be, not to restrict or increase this one or that one, but to make all approach as closely as we can to the proper standards; and this is done by suitably altering the kinds of individual food-articles that the patient takes, and from which he secures his protein, fat, and carbohydrate. One's skill in doing this will depend chiefly upon knowledge of the constitution of foods, and upon the care with which one arranges the details of the foods permitted. When a diet-list is once formulated, it should be inspected to see whether the amounts of these substances are made to approach reasonably closely to the normal; and if they do not, one should attempt to alter them in such a way that they will.

We know clearly the absolute necessity for a certain considerable quantity of protein. This our tissues absolutely demand. As I have already stated, I think the amount desirable approaches the

older standards. We have equally good grounds for believing that an excess of protein is decidedly undesirable, because of the extra tax that it imposes upon the metabolic and excretory organs; for the breaking-down and excretion of protein is, with most persons, somewhat more difficult than is the same process with fats and carbohydrates.

An excess of carbohydrates is, as everyone knows, likely to be harmful in its effects upon digestion; and it is highly probable that an originally normal carbohydrate metabolism may be overtaxed by an excess. We know most convincingly, at the present day, that a decided restriction in carbohydrates is harmful, and may even be productive of grave toxic symptoms—chiefly through the production of acid intoxication.

An excess of fats is a very common cause of digestive disturbance, particularly of disorder of the stomach; and, when associated with a reduction of the carbohydrates, readily produces more or less serious acid intoxication through metabolic disturbance. While the effect of a marked reduction of fats may be directly harmful, we do not know this; but we do know that with many persons it is indirectly harmful, in that it leads to the necessity for taking a large excess of protein or carbohydrate, or both, in order to replace the great food-loss that goes with a considerable reduction of the fats.

This point in regard to the fats is, I think, worthy of a little more emphasis, because it is not commonly appreciated sufficiently. I shall be brief, however; because I have recently written at some length regarding the evil effects of fats.[2] Everyone knows that fats are very nutritious, but I think that the extent of this fact is not often realized. Their high calorific value (9.3 per gram, as compared with 4.1 for either carbohydrate or protein) and the fact that fatty foods are usually extremely concentrated, while both carbohydrate and protein foods usually contain a great deal of water, make fatty foods, as they are ordinarily served, exceptionally valuable sources of concentrated nourishment. As instances, I would mention the fact that a given portion of butter has eight or more times the value of an equal weight of lean beef-steak; olive oil has an even higher relative value; and a pint of good cream contains a fairly generous half-day's ration for any one of us, nine-tenths of

[2] Boston *Med. and Surg. Jour.*, Dec. 27, 1906.

this being due to the fat. This makes apparent the reason for the free use of cream, rich milk, butter, olive oil, rich cheeses, and such foods, when one is treating patients that need generous feeding. Fats have, therefore, an enormous value as foods, particularly when some other foods can be taken but sparingly; and in diabetes, they are our chief resource. In diabetes, however, they are our chief danger also; and in many other conditions they produce untoward symptoms, owing at times, to peculiarities in the individual, either inherent or acquired through disease; at times, to their use in indigestible form or in irrationally large amounts.

In these present days, in which the frequent value of free feeding is constantly growing to be more and more thoroughly recognized, one has to be on one's guard continually against the results of overburdening patients that have been freely fed by one's self or one's professional brethren; and I think that the evil effects of excessive quantities of fats are met with quite as frequently as bad effects from either protein or carbohydrate. Indeed, I believe that they are, if anything, more common. One should know with a fair degree of accuracy how much fat one is ordering. The gross errors that may be committed by loosely ordering patients to take fatty foods freely are exampled by a case that I mentioned in the paper referred to above: a boy of eleven years, who was taking two hundred and fifty to three hundred or more grams of fat per diem, —about three times the amount that a normal man ordinarily takes. His parents had been told to "feed him up."

There are, however, some conditions in which one finds it desirable or even necessary to reduce the amount of one of these particular main classes of food. The protein should be kept at a relatively low point, although, in my opinion, it should be only moderately restricted, in cases of hepatic, renal, circulatory, and indefinite metabolic disease, in order to keep within bounds the labors of the already overtaxed organs. I think a still more important point is to keep the total protein reasonably near the normal point, but to be careful to reduce the kinds of protein that yield products that are particularly difficult to break down and excrete; that is, more especially, those kinds that contain much nucleoprotein and extractives. One should, namely, exclude organs, such as liver, kidneys, and sweetbreads; should keep meats and

leguminous vegetables within moderately narrow bounds; but should use with proper freedom milk, eggs, and other protein-rich foods that cause little labor in their passage through the body.

When there is digestive difficulty in taking carbohydrates, there is, I think, a too general tendency merely to reduce the amount of carbohydrate. Ordinarily, I find it comparatively easy to give a great deal of carbohydrate in such cases, provided the more easily digested kinds are used—such kinds as doubly-baked breads of various sorts, long-cooked and strained gruels, or dextrinized gruels, and those carbohydrates, such as rice, for example, which are quickly digested before they have much opportunity to undergo fermentation, and leave little irritating residue in the digestive tract.

When there is difficulty in taking fats, we are much more restricted in our choice from the standpoint of digestibility, and are often driven to a more or less prolonged reduction of the amount taken. Often, as is well known, the milk-fats are acceptable when others are not; but in my experience, they are by no means so commonly found digestible as is ordinarily taught, and I think that many persons have, for some time at least, an intolerance for any noteworthy amount of even milk-fats. A proper manner of preparing some fats, which will make them both acceptable to the palate and more digestible, as, for instance, a proper manner of preparing bacon, will sometimes overcome the difficulties in using them.

I wish to speak but hastily of a very few further points: First of all, I would mention the necessity of carefully watching the supply of fluid. It is quite apparent, although it is not sufficiently appreciated, that bulk is taxing to the digestive, circulatory, and excretory organs; and if one wishes to spare any or all of these organs, one should know exactly what bulk the patient is getting and should keep it within proper bounds. Fluids, of course, make up most of the bulk. We now know well, for instance, that in kidney disease, in which circulatory failure is one of the chief dangers to be guarded against, a long-continued liquid-diet is by no means the mild and benign measure it was long considered to be. In such cases, excess must be guarded against. On the other hand, it is no less commonly desirable, especially in infectious toxemias and in disorders of metabolism and excretion, to see to it that the

amount of fluid does not fall below the normal; and it may often, with profit, be kept moderately above the normal. There is a growing, but, as yet, not sufficiently general, understanding of the value of keeping patients of the kinds that I have just mentioned moderately flushed. Common sense would indicate, and both experiment and clinical experience demonstrate, that increasing the quantity of solvent increases the amount of substances carried out in solution, and therefore reduces the toxemia. I believe, also, from my own studies and those of others, that free water-drinking distinctly increases the activity of metabolism, and that this effect may be continued for a long time. The practical point upon which I would insist in this connection is that when one wishes to flush a person, it is not sufficient to tell him to take a certain amount of fluid; it is necessary, also, to have the amount of urine passed in twenty-four hours recorded, occasionally, at least. Sweating may so reduce the amount of urine that the latter falls even below the normal, in spite of the fact that the patient may be taking large quantities of water. Flushing through the kidneys is much more efficient than flushing through the skin, and the only way of determining how satisfactory the kidney-flushing is, is to measure the twenty-four hours' urine and to push the intake of fluid in accordance with this. I have seen cases in which in summer time it was necessary to use as much as five or six quarts of fluid daily in order to get the urine up to the two quarts or so that I desired them to pass; and they improved only when this was done.

I would mention one or two other considerations: It occasionally becomes necessary to spare the digestive organs much of the work of digestion by using predigested foods, and at times the stomach is so rebellious as to make it necessary to introduce food through other channels. As to predigestion, I would say that it is but rarely necessary, if one acquires and uses some skill in choosing foods that are sufficiently bland in their general character and have a constitution suited to the individual case. I think that much less success comes from a ready recourse to predigestion, with the idea that the digestive organs are simply too weak to do their work properly, than from a careful consideration of the elements of the diet in general and of the individual food-articles in particular, with the idea that some one of these elements may be at fault.

This is clearly shown to be true in pediatric practice. When a milk-mixture disagrees with an infant, one would not, as a rule, advance very far, if one simply hastened to predigest the milk. One needs to find out the element in the milk that is at fault. The same thing applies to adults. I think that unmodified milk often disagrees with adults, in spite of many medical denials of this statement; but I have rarely found predigestion necessary, and it has been extremely disappointing in many cases in which I have tried it. At the same time I think that almost anyone can take milk, when properly administered, if one determines, in the first place, that it is not infected milk; and, in the second place, whether the fat or the casein may not be causing the difficulty in some manner that can easily be corrected. I have found that reducing the fat by partial or complete skimming or, in case the casein is at fault, reducing the amount of this substance or adding a gruel, is much more helpful in making milk acceptable than is mere predigestion. There is too common a tendency, I think, to hasten to predigestion, when in difficulties. One direct disadvantage of this measure is that if the digestive functions are not normally exercised, improvement may, to be sure, result as a consequence of the rest, but if the predigestion is long continued it is at times a difficult and laborious process to educate these organs to do their proper duties again.

There is another side to this subject, however: When one is obliged to use predigestion, and also in the much more frequent cases in which one must, for a long time, use a very simple diet, one often meets with mild or somewhat severe rebellion on the part of the digestive organs when one attempts to give them more difficult or more complex work to do. This is not by any means always an indication for renewed care. One's muscles grow painful from the first exercise after a prolonged rest; and this simply indicates the necessity for gently increased exercise, not for cessation of exercise. This point in dietetics, however, is one that requires nice discrimination in the individual case.

In regard to the necessity for introducing food by abnormal channels, that is chiefly per rectum, I would only repeat quite briefly what I have previously written; namely, that one should have a clear conception of what one is doing in such cases. The studies that I have made of absorption and metabolism in exclu-

sive rectal feeding, together with the work of others, have made it clear to my mind that when one cannot feed a patient by the mouth, one's best efforts by other means are usually so unsatisfactory that the condition must nearly always be considered to be dangerous; and one should always be on the alert, in such cases, to use the proper channel again, if possible, or to subject the patient as early as possible to any contemplated operative measures to relieve the condition.

It would be easy when dealing with so extensive a subject as that included under my title to continue to elaborate indefinitely even though one confined himself to the bounds of general principles. My purpose has been to outline merely the preliminary skirmishing that decides the manner of attack. The chief points that have helped me have been an increasing appreciation of the value of great accuracy in determining what the patient is doing by himself whether right or wrong, and what we are doing when we regulate his diet; in the second place to start as a rule with a rest and with simplicity, but to be on our guard lest our restrictions, while causing special symptoms to improve, do the patient general damage; in the third place to acquire some knowledge of the constitution of foods and of their behavior in the body, so far as these points are known, and to apply this knowledge to individual patients and the disordered conditions that they present, not to names of diseases or to theories; in the fourth place to choose foods with the idea that a wide departure from the normal in total amounts or in the amounts of the three great classes of foods is disadvantageous—that difficulties should not be met by mere reduction of the total amount of food or of the amount of one of the general classes of foods, but so far as possible by substituting for the troublesome members of a class others of the same general class that yield a different digestive or metabolic residue or may be so prepared as to be more suitable; and finally to determine not only what should be done about the foods, but what may wisely be altered in the habits of eating and in the use of fluids and food accessories such as condiments, salts, and stimulants.

If in presenting these points I have not discussed them in so elementary a way as to have appeared to do insult to your intelligence I shall be satisfied.

# ON THE TREATMENT OF PNEUMONIA, AND ESPECIALLY THE ACTION OF METALLIC FERMENTS IN THIS DISORDER *

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It is not an exaggeration to say that at the present time there exists no treatment for pneumonia. The infectious agent of the disease has been discovered; we appear to know all about the pathological anatomy; there is not a detail in the clinical history or even in the pathological chemistry that does not seem to have been thoroughly investigated; finally, the pathogenesis has been deduced, with apparently the closest logic, from everything that modern science has discovered in this connection,—and the outcome of all the foregoing has been,—both in private and in hospital practice,—no more than the therapeutic delusion that has been called "armed expectation."

This attitude of armed expectation is, in reality, no more than an avowal of our helplessness in the face of this disease, since we thereby abandon it to its natural evolution, refrain rigorously from using any direct means against it, and limit ourselves to moderating predominant symptoms, checking complications, and keeping up the patients' strength.

This course of action, then, takes little notice of the disease itself, but merely hovers on its outskirts, while being influenced by any theories that may be prevalent or by the drug that happens to be foremost at the time.

Attempts have, of course, been made to arrive at an etiological and pathogenic therapeusis of pneumonia; but although the results at first seemed promising, the actual results of such methods have proved disappointing, so that we can say that every effort made

* On the same subject *vide* Albert Robin, INTERNATIONAL CLINICS, Fifteenth Series, vol. iii, p. 39.

either to immunize the body, by the pneumococcus directly or indirectly, or to attenuate the virulence or moderate the reproduction of the pneumococcus, has failed entirely. And this is equally true of the serum treatment of this disease. Those who have tried to combat the pneumonic lesion itself, as well as those who, considering this lesion as a secondary manifestation of the infection, have endeavored to throttle the one or the other, have all been forced to recognize the failure of their efforts.

At the present time, and in spite of the immense efforts that have been devoted to this subject, the treatment of pneumonia is reduced to the treatment of the predominating symptom. What is done is to control the pyrexia with quinine, antipyrin, or pyramidon; to relieve pain in the side with morphia injections or wet cups; to bleed, sometimes, robust and congestive cases; to facilitate expectoration with preparations of antimony; to raise vascular tension and quiet the pulse with digitalis; to give emetics in bilious cases, and alcohol and cinchona in adynamic cases; to inject caffeine when the pulse is soft, weak, and irregular; to prescribe potassium bromide for delirium, and to bathe the ataxo-hyperthermic patients. And when stress is laid, very properly, on the necessity for maintaining diuresis, it is with the very elementary notion of helping the elimination of toxins. As for blisters, although they still enjoy the favor of the public and of the practitioners, the greater part of the teaching portion of the profession disapproves of them altogether.

Such being the state of the case, the idea occurred to me to see whether it would not be well to look for some other line of action capable of leading to a rational treatment of pneumonia, and in particular whether there might not be found in the course of *organic exchanges,* during this disease, some element that might guide our treatment. In doing this I shall rely solely on my own researches, though many others have been made in this direction.

A first point of importance is, that, during the defervescent period of pneumonia, and sometimes even at the beginning of that period, a discharge of urea or of uric acid quite frequently takes place and appears to characterize the crisis. Such a discharge may sometimes be very considerable, 40 grams of urea and more than 1 gram of uric acid, for instance, in twenty-four hours. Take a case of pneumonia with such a serious complexus of symp-

toms that the probable outcome is uncertain and the patient's condition justifies the greatest anxiety. If at such a moment the addition of nitric acid to the urine causes a heavy disc of urea nitrate to form, that is, if the discharge of urea is equal to 40 grams per litre, we can be sure, at least in most cases, that defervescence is at hand, and that it will occur during the next twenty-four or forty-eight hours, no matter how serious the symptoms may be.

This occurrence is not constant, however, even in serious cases; and there are instances where defervescence is accompanied by a simple discharge of uric acid, or even without either urea or uric acid. Still, these *precritical discharges* are common enough to be considered, in a way, as the rule.

In the next place let us examine the elimination of the total amount of nitrogen of the urine, comparing it with the urea. This ratio in the normal is 85 per cent. (urea to total nitrogen). Now, it will be found that in fatal hypertoxic cases this *coefficient* is noticeably less, descending to between 68 and 73 per cent. on an average. Let us see what happens in this respect when the disease ends in recovery. Never have I seen, as far as I know, this coefficient so low in recovery as in fatal cases, and a ratio of 72–75 per cent. is a rare exception. Usually 77–82 per cent. is the figure at the height of the disease, rising noticeably during defervescence.

The type of the elimination of urinary nitrogen in pneumonia offers many exceptions, and it is not usual for the curves of the daily coefficients of two patients to be at all alike. But it is none the less true that most simple cases of pneumonia follow the rule we have mentioned, and that consequently the pneumonic crisis coincides with an increase of all of the hydrating and oxido-reducing chemical acts which indicate the vigor with which the system defends itself, and are in this way one of the essential conditions of the salutory crisis.

At first sight, and in view of former ideas concerning the formation of urea in the system, we might be tempted to look on the increase in this coefficient during convalescence as denoting more active oxidation of albuminoid matter, than of the morbid and toxic products of its disintegration. But we now know that urea is a product of reducing acts, and not of directly oxidizing ones. There ought rightly, therefore, to be no relation between the amount of

urea formed and eliminated, on the one hand, and the consumption of the oxygen inspired, on the other, since we have always been taught, on the contrary, that oxidation increases during the defervescence of pneumonia.

The comparative examination of respiratory exchange during pneumonia and during its defervescence confirms the modern view as to the source of urea. For the total consumption of oxygen per kilo of weight and per minute is less during defervescence than during the height of the disease; and what decreases in particular is the oxygen used by the tissues, that, namely, which does not contribute in forming $CO_2$. It is clear from comparing general exchange and respiratory exchange during pneumonia that the increase in urea and its co-efficient, so far from coinciding with a parallel increase in respiratory exchange, goes rather with a decrease in the latter.

These acts require neither total consumption of a greater quantity of oxygen, the formation of $CO_2$ in excess, nor even the absorption by the tissues of a larger proportion of oxygen, which proves at any rate that this oxygen takes no direct part in them. Furthermore, since the consumption of oxygen decreases at the time of crisis, we have almost a right to think that oxygen consumption is rather unfavorable to elimination than otherwise, that these phenomena occur with greater vigor when oxygen consumption lessens, and that this very diminution is one of the conditions favoring urea exeretion.

The spontaneous crisis in pneumonia has, therefore, as immediate condition if not cause, not acts of direct oxidation, but acts of oxido-reducing hydratation, which denote the reactional method of defence of the body against pneumococcic infection, and whose essential agents are the diastases set at liberty by the intense destruction of leucocytes that occurs at the same moment. The drop in temperature, discharge of urea and uric acid, and the increase in coefficient, are the external manifestations of the two internal acts of general exchange. It often happens that these discharges take place before the fall of temperature, apparently while the disease is still in full course, whence the name of precritical discharges. They have, then, the prognostic value to which I referred, and the art of therapeutics should consist in giving rise at the proper

moment to the spontaneously curative chemical acts which they express, and to help them when they are insufficient.

We find ourselves, then, far removed from the guiding ideas of classical therapeutics, the chief of which objective is to fight the disease; for the leading indication that we are now to follow consists solely in favoring the system's natural tendency to recovery. We have, therefore, to find therapeutic agents capable of bringing this tendency into play.

In former works, I have shown that exact similitude exists between the chemical phenomena denoting the defensive reaction of the system in pneumonia, and those aroused by hydrating and oxido-reducing diastases, such as sera and metallic ferments. We were, therefore, entitled to think that these favorable chemical phenomena might be produced, assisted, or increased by the therapeutic use of these different agents, and especially by metallic ferments, whose action is precisely similar to that of diastases and sera, without giving rise to the drawbacks the latter so often have.

These phenomena can be rapidly summed up as follows: The total nitrogen, urea, uric acid, and coefficient increase after an injection of metallic ferments; the maximum of this increase occurs between twenty-four and seventy-two hours after the injection. While this increase is taking place, regular variations can be noted in respiratory exchange, of which the following are the principal ones: *First:* The oxygen consumed by the tissues lessens six hours after the injection, and this decrease becomes more marked still in twenty-four hours. *Second:* The respiratory quotient rises regularly, from 6.7 to 9.7 per cent. six hours after the injection, and from 8 to 13 per cent. after twenty-four hours. *Third:* The $CO_2$ produced and the total oxygen consumed vary more or less according to the differences between cases. Nevertheless, it should be noted that the total oxygen consumed has a tendency to lessen, that it always lessens more than the $CO_2$, and that when it increases it always does so to a smaller degree than the latter.

Metallic ferments, therefore, lessen the total consumption of oxygen, without lessening to an equal degree, even sometimes increasing, the production of $CO_2$, so that the result is that there is a constant reduction of the oxygen consumed by the tissues, which raises by so much the respiratory quotient. Consequently, by comparing

general and respiratory exchange we are necessarily led to the conclusion, that metallic ferments increase the acts of oxido-reducing hydratation of the system, since the total nitrogen and the urea increase at the exact time that the total consumption of oxygen, and particularly of the oxygen consumed by the tissues, decreases. They, therefore, improve the evolution of disintegrated nitrogen, and appear to moderate the oxidation of ternary substances.

The analogy between the remote phenomena of the pneumonic crisis, and the different effects on the system produced by metallic ferments, is shown still farther by the study of the blood tension and of the temperature; but as I have treated this side of the question elsewhere I need not repeat it now.

It was this analogy between the effects of metallic ferments and the spontaneous chemical acts of the pneumonic crisis that led me to try to apply them in therapeutics. This species of treatment belongs rather to the Hippocratic school than to that of Galen, whose object was to attack directly the disease itself. On the one hand, we are familiar with the correlative chemical acts of the natural crisis, and on the other, we are in possession of substances capable of giving rise to these chemical acts: was it not rational to try their use in clinical medicine, particularly since experimentation had shown me their entire innocuity?

For 5 years I have been carrying out these experiments, and with good results. As an example let me cite the following instance: A man of twenty-six, with the alcohol habit to a marked degree, was seized with fever and a rigor during the night of the 7th to the 8th, and on the 9th was brought to the hospital in a condition of great depression, interrupted by periods of delirious agitation; respirations were 54 per minute, pulse 104, temperature 39.3° C. The left lung, dull in its lower three-quarters, showed blowing sounds with volleys of crepitant râles. On the morning of the 10th, the temperature was 39.9° C.—in the evening, 40.3° C.; pulse and respiration remained unchanged. Urine contained much albumin. Left lung unchanged. Râles of scattered bronchitis found on the right side; tongue dry and black. Heart contraction weak, sounds dull. Treatment consisted of stimulants and wet cups.

On the 11th, morning temperature was 40.2° C., evening 40.4° C., pulse 118, respiration 56. Condition was much worse. Tongue

was wasted. Sputum was in great quantity and abundant, and showed black patches as at beginning of gray hepatization. An injection of 10 c.c. of palladium hydrosol was ordered. In the evening the condition was still doubtful, the local symptoms had not changed; two hours after the injection a discharge of uric acid and indoxyl occurred, which was still noticeable four hours later. At the sixth hour these elements tended to decrease, whereas the albumin visibly increased; twenty-four hours later the albumin had disappeared, but the indoxyl was still visible.

On the 12th, as no improvement had manifested itself and as the situation seemed even more serious than the previous day, the pulse being 124, another injection was made. That evening the temperature was slightly lower, but the pulse had fallen to 90 and the respiration to 48, the patient having fallen asleep bathed in perspiration. Three hours after the injection a high amount of uric acid was thrown off, with traces of albumin and a little indoxyl. Eight hours later the excretion of uric acid was still persisting, with an increase in indoxyl. Twelve hours later the urine treated with nitric acid showed a dense disc of urea nitrate.

On the 13th, the improvement, begun the previous afternoon, continued rapidly, with intense sweating; the temperature fell to normal, patient felt better and the tongue became moist. Convalescence proceeded uneventfully, and the patient left the hospital on the 22d, just sixteen days after the beginning of his illness.

This patient may be taken as a type to which most of my other cases correspond. From a comparative examination of the cases a certain number of points which seem worthy of notice can be gathered. The injection of metallic ferments produces almost always a rise in temperature, beginning after an hour, increasing for six or eight hours, and reaching its maximum from the sixth to the tenth hour. This maximum, very variable, oscillates between a few tenths of a degree and a degree and a half centigrade. It is followed by a descent, which brings the temperature noticeably below the point at which it stood when the injection was made. In some cases the effect of the injection on the temperature is irregular, but these are exceptions.

If, now, we consider the effect of these injections, not on the immediate temperature, but on its general tracing, we note almost

always a decrease, the duration and intensity of which varies according to the stage of the disorder at which the injections are made, and, also, according to the issue of the case. When the injection is made at the start, the temperature decrease is less regular, and when this fall of temperature occurs it does not last. But by repeating the injection daily, the drop in temperature occurs visibly sooner than in cases not treated in this way. Thus, in 38 cases I observed that the final temperature drop occurred on the eighth day in 63 per cent. It was abrupt with most of the patients, with a drop of from 2.5 to 3.5° C. The drop, therefore, in cases treated by metallic forments is both early and rapid.

In cases ending in death the temperature shows on the day after the injection a less constant and always temporary decrease. In some cases the temperature is not influenced at all. As to the hourly modifications of temperature after the injection, the curve is quite different from what it is in favorable cases: the rise following the injection is more rapid, greater, and does not end in defervescence. When the latter takes place it is unimportant and temporary. Pulse and respiration follow the course of the temperature.

An injection of metallic ferments usually increases arterial tension, and this increase is a favorable sign. In ordinary cases of pneumonia, decrease in tension is usually a bad sign; when during the height of the disease tension keeps at the normal, the disease has a greater chance to go to recovery. Tension usually decreases during defervescence, to rise again at the end of convalescence. Under the influence of the metallic ferments (gold, silver, platinum, palladium, manganese) tension is raised more or less visibly, and its descent is not always coincident with defervescence, although it generally occurs in the course of the latter.

The urinary reaction, characterized by increase in uric acid, indoxyl, and by the formation of a disc of urea nitrate, is constant in at least one of its elements: increase in uric acid is, one may say, never absent. As for the disc of urea nitrate, it appears in about half the number of cases. Amelioration in the principal symptoms of pneumonia is in direct relation to this reaction, which is most unusual in cases that end fatally.

Albuminuria, so common in pneumonia, increases sometimes in one or several of the specimens of urine following an injection. It

is not unusual, indeed, to observe traces of albumin in the urine of patients who, before the injection, had shown none at all. But in either event, this albuminuria disappears rapidly, and in none of our cases was it found to persist after defervescence. Often when there is albuminuria in pneumonia the injection causes this symptom to disappear in twenty-four hours.

In several of my cases, sudden defervescence was followed, in a few days, by a fresh rise of temperature, which, however, immediately yielded to a new injection. I have also remarked in many cases that the crisis of polyuria, which generally occurs at or about defervescence, was more or less retarded. Thus, with one patient it did not appear till the thirteenth day, defervescence having taken place on the seventh. In another, defervescence showed itself on the fifth day, but the polyuric crisis only on the tenth.

There remains now for me to give my statistical results in treating pneumonia by metallic ferments. In the 53 cases that have passed through my hands 47 recovered and 6 died,—11.32 per cent. of deaths, one of the lowest percentages ever reported; it is even the lowest, and by a great deal, if we consider that among these 53 cases there were 26 very serious ones, and also that all were hospital cases, most of them complicated with alcoholism, and treated as a general thing at an advanced period of their disease. The 6 who succumbed were all desperate cases, most of them alcoholic, several of them with complications in other organs, who died more or less rapidly in spite of all our efforts, and in spite of injections of different metallic ferments,—manganese, gold, and palladium.

The foregoing cases, and the post-mortems of several patients, show that the metallic ferments have no action on the pneumonic lesion itself, but on what the school of Montpellier called the pneumonic fever. They stimulate the reactions of organic defence against the intoxication and its products, by making more active the hydrating and oxido-reducing evolution that transforms the latter, makes them soluble, and reduces their power of doing harm. They are a means of helping the *vis medicatrix,* of reinforcing it, perhaps of giving rise to it; but, owing to the number of elements which go to form the high death rate in pneumonia, they can by no means be looked on as the only method of treatment to be employed.

Their usefulness consists solely in that they act in the same

manner as the system itself in its normal defence. They superpose to the vital and personal reactions of the body, a parallel activity which manifests its effect in the quicker disappearance of the general symptoms correlative to the infection. But they must not lead us to neglect the other therapeutic means, which time has proved to be efficacious, without explaining in what manner. Consequently the ferments must be considered only as one of the elements in the treatment of pneumonia, which I shall attempt to outline for cases free from complications. Special involvement of an important organ, such as the liver or heart, implies at once a special set of indications to be filled at the same time as those resulting from the evolution of the disease itself. It is the latter alone that I am considering at present.

When a patient with pneumonia is vigorous and has been seized in the midst of good health; when his face is congested, pulse full and strong, temperature high, and there is much dyspnœa; he should first be bled, 300–400 grams from the arm, with the intent to create a slight degree of circulatory depression, but particularly to favor respiratory exchange, which lessens the dyspnœa. In all other cases bleeding is inadvisable. Bleeding is much preferable to wet cups, so extensively used to-day as to form a routine method of treatment in our hospitals. No doubt they are more particularly prescribed for patients who have violent pain in the side; but even so, they never produce the relief that can be obtained from a hypodermic injection of one-half or 1 centigram of morphine. On the other hand, as regards their action on respiratory exchange, it is too unimportant to have any real effect on the dyspnœa, when the latter is very marked. At the same time a stimulating draught containing 60 grams of rum should be given, of which a tablespoonful can be taken every two hours. In the way of food, milk and bouillon are to be given, especially the former, of which from 1 to 2 litres should be taken during every twenty-four hours. Since the amount of alcohol in 60 grams of rum is insufficient in many cases, and particularly in hospital ones, the quantity necessary, which corresponds to about 100 grams of rum, can be made up either by adding a teaspoonful of cognac to each cup of milk, or by giving grog or champagne with water.

Morning and evening until defervescence the patient must take 0.30 grams of bi-chlorhydrate of quinine.

The day following the bleeding, or at the start when no bleeding is done, 0.40 grams of calomel should be prescribed, 4 powders of 0.10 grams, taken at intervals of an hour, for the purpose of setting up intestinal elimination, manifesting itself by two or three loose stools with no diminution in diuresis.

Twenty-four hours after the calomel, the first hypodermic of metallic ferment should be given (10 c.c. of gold, silver, platinum, palladium, etc.). I have often had occasion to use manganese organosol in the same dose. This preparation appeared to me sometimes more active, but it is difficult to prepare, which renders its use less practical. As for the metallic hydrosols, which I have tried, they do not seem to differ in their activity. The injection should be repeated every forty-eight hours, and should be made in the neighborhood of the local process, though place should be allowed for the blister to which reference will be made presently. In very grave cases an intravenous injection of 5 c.c. of the metallic ferment should be made. The day following each injection, at evening, together with the normal dose of quinine, a wafer of 0.30 grams of pyramidon should be given. This combination of remedies, applied in this manner, produces profuse sweating, sometimes extremely abundant, requiring several changes of linen, which must be effected with every precaution against cold.

Finally, twenty-four hours after the first or second injection, but in any case not before the fourth day of the disease, a large blister, 10 cm. by 10 cm., well sprinkled with camphor, should be applied over the lesion, but only left in place eight hours, after which it should be carefully removed and the subjacent skin, now red and irritated, covered with an ample flaxseed poultice under which the blisters can form without pain. At the same time all irritation of the kidneys by cantharides is avoided.

This outline gives what might be called the functional treatment of pneumonia, as I understand it, since no one of the elements of which it consists pretends to have any direct curative action, in the classical sense of the term. No one of them takes into consideration the pathogenesis or causation of the disease, not even the calomel, which is only given here as an evacuant and derivative, without any attempt at an antiseptic effect.

This treatment does not combat the disease; it is exclusively

addressed to the functional reactions of the system against the morbid agent and its manner of attack. We know that a patient with pneumonia defends himself by raising to a maximum the acts of oxido-reducing hydratation of which the tissues are the seat; we know that the leucocytes play in the accomplishing of these acts an important part, and without looking any farther or trying to interpret these phenomena, we rest content with increasing the hydrating and oxido-reducing processes as well as the activity of the leucocytes.

We know that before the crisis of pneumonia the respiratory exchanges have a tendency to rise, which is in relation with the greater intensity of the oxidations at this period of the disease, and we help on this spontaneous act, on the part of the system, by a removal of blood. The quinine is given simply as a general tonic. The combining of it and pyramidon, after the fourth day of the disease, prepares the way for the sweat crisis that habitually appears at about the time of the defervescence.

Reduced to this rank as an assistant of the *vis medicatrix*, merely helping the patient to get well, this functional treatment does not pretend to assume the entire burden of the treatment of pneumonia. But it represents the fundamental element, about which can be grouped, when necessary, the various methods of treatment that may be necessitated by the appearance of a complication, by the predominance of some abnormal symptom, or by some peculiarity in the lesion itself.

I have taken care of 13 cases of secondary bronchopneumonia, all very serious ones, of which I lost 6, or 46 per cent. The first was a woman of eighty, stricken with bronchopneumonia produced by grippe, who died twenty-four hours after entering our wards. No. 2, 3, and 4 were similar cases, with disseminated foci in both lungs—two men, thirty-four and sixty-eight years of age, and a woman of fifty-four, who after being treated in the regular manner succumbed, on the twenty-first day. The others died on the fifth and ninth days of disease. No. 5 and 6 had double pleurobronchopneumonia, also of influenzal origin—two women of thirty-eight and forty-two. They died on the eleventh and twelfth days.

Of the 7 recoveries 3 were men, forty, forty-five, and fifty-nine years old, stricken with serious bronchopneumonia caused by grippe,

and another, a man of fifty-three, seized with bronchopneumonia during chronic nephritis. Defervescence occurred with him on the sixth day, after 2 injections of manganese organosol. There were 3 women, thirty-three, thirty-six, and sixty-nine years old, who were very seriously ill. In the one of sixty-nine defervescence occurred on the twelfth day, after 2 injections of silver. For nine days her temperature remained normal, but then she had a relapse, with a temperature of 40.1° C., which yielded in seven days to 2 more injections of silver.

The number of these cases treated is too small and their gravity too unusual for me to draw statistical conclusions, but it appears that the metallic ferments are less efficacious in serious cases of bronchopneumonia. The urinary reactions and the formation of the urea nitrate disc, in particular, are more rarely observed in these cases than in ordinary pneumonia of no matter what severity.

I have no doubt that the objection will be made that pneumonia is a disease with a brusque defervescence and cyclical evolution, and that the cases treated after the foregoing plan have done nothing but follow the usual law. But it is easy to reply to this objection. Even in simple cases defervescence rarely occurs before the eighth day, whereas in our cases it usually took place at an earlier time. Again, the low death rate of my series, in spite of the fact that it contains 26 serious cases, is another argument in favor of the efficacy of this treatment. Finally, the regularity of a descent in temperature after the injections, as well as the rapidity of defervescence, are also clinical arguments that have their value.

I expect at some future period, in connection with the treatment of cardiac complications in acute muscular rheumatism and of non-tubercular forms of meningitis by metallic ferments, to show that the latter have the same effect in these disorders as in pneumonia, and consequently that the argument of the cyclical evolution has no foundation. This similarity in action enables me to suggest a very plausible hypothesis,—this is, that the process employed by the system to defend itself against toxic infections, is connected with acts which may be different in origin and manifestations, but whose final outcome is an increase in the phenomena of oxido-reducing hydratation that intervene normally in the processes of disintegration and final evolution of albuminoid matter.

# MECHANOTHERAPY

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Rubbing has been in use from times immemorial. Kong Fu, a Chinese writer, about 2700 B.C., gave a full description of medical gymnastics and massage as then practised. That the ancient inhabitants of India were acquainted with these means of treating disease and of preserving health is shown by the mention made of gymnastics and massage in the Hindu Vedas.

Massage was practised in Persia, Phœnicia and in Egypt, while the ancient Greeks used massage largely. Hippocrates advocated massage. The Romans learned its use from the Greeks, and fully recognized its value as a luxury and as a therapeutic measure.

In the latter days of the Roman Empire baths and massage were widely employed. The literature of Rome teems with references to the value of massage from a medical point of view. It eventually fell into disrepute with the medical profession in Egypt, Greece and Rome, on account of the abuses to which the method led. For the same reasons a prejudice has sprung up against its use in America and in Great Britain.

Massage treatment was abandoned after the fall of the Roman Empire until the end of the seventeenth century, and it was not until the nineteenth century that it was really revived and placed on a medical and scientific basis by the Swede, Ling.

Ling was a teacher of gymnastics and fencing in the University of Lund, and founded, in 1813, the Central Gymnastic Institution in Stockholm. His medical gymnastics were propagated and developed throughout Europe. It is most used in Sweden, Germany, Holland, Austria, Denmark and Norway and is also used to some extent in France. It is recognized in Russia but almost unknown in the southern European countries. In Great Britain the method is in its swaddling clothes, owing perhaps to the fact that its exponents are persons of no education, and that as a therapeutic meas-

ure it has not been taken up by the medical profession. In America mechanotherapy is also in its infancy and here, as in Great Britain, the medical profession is inclined for the most part to look askance at the mode of treatment, and to imagine that a popularization of the method would open the door to quacks and others who might injure their interests.

In the countries of Europe, however, in which mechanotherapy is largely practised, the method is recognized as a legitimate and valuable part of medical treatment. The masseurs and gymnasts work under the direction of a physician, and when a medical practitioner has satisfied himself that a masseur is in every way competent to practice the method, he sends the patient to him and only supervises the treatment.

With a clearer understanding of how nature effects a cure and maintains health these various forms of motion, in imitation of the physiological workings of the body, may be very potent therapeutic factors.

During massage the patient is to occupy a position of ease. The part to be subjected to massage must first be thoroughly cleansed and the same holds good for the hand of the operator. At no time should any of the motions be violent, and to lessen the effects of friction on the skin, a small quantity of lubricant is in place. Vaselin, cocoa-butter and talcum powder answer best.

Massage embraces the motions known as Friction, Kneading, Percussion, Stretching, Pressure, Vibration, Stroking. In the execution of these, the general rule should be observed that the motion be carried out in a centrifugal direction, *i.e.,* always favoring the circulation of fluids of the tissues from the periphery to the centre of the body.

*Friction* may be executed with the entire hand or with one or more fingers. In the former case it is palmar friction, in the latter digital. These friction movements are performed alternately with each hand in more or less rhythmical succession. Friction generally introduces the seance of massage. Its purpose is to open the pores of the skin, favor the capillary circulation, and stimulate the peripheral nervous system.

*Kneading,* again, may be carried out with the entire hand (palmar), or with a few fingers (digital). Kneading is the term

borrowed from the similarity of this manipulation to that of bakers in handling dough. This modified form of friction is intended to reach the deeper parts—muscles, intestines, glands and nerves.

Palmar kneading is reserved for the manipulation of groups of muscles, as in the kneading of an entire extremity. This motion is to be executed by moving the hands in opposite directions and letting the muscles, embraced with moderate, uniform pressure, gradually escape from their grasp.

In like manner digital kneading is performed by grasping with the fingers single muscles, and not unlike the act of pinching, permitting their escape. For muscles at least, palmar and digital kneading ought to be executed from the point of muscle origin to its insertion. In the application of digital kneading to the intestine the abdominal muscles must be absolutely relaxed, and this kneading of course must be in the direction of the alimentary and fœcal circulation—from the stomach towards the rectum. The breast and uterus may be kneaded by a continued action of the palm and fingers of one or both hands.

*Percussion* generally succeeds kneading. It comprises a succession of sharp blows delivered with the flat of the hand (palmar), the *ulnar percussion* executed with the ulnar margin of the hand, digital percussion delivered by the tips of the fingers. To smart blows given by the dorsal surface of the fingers of clenched fist the term *dorsal percussion* is applied. The motion of *ulnar percussion* is akin to that of chopping meat with cleavers. This motion of percussion being more forcible, is to be reserved for the more fleshy parts of the body; the trunk, in the loin, buttock, thigh, along the spine, nape of the neck, pericardial area, and thorax.

*Stretching* is next in order. It consists in applying extension to the various extremities. It has a limited application, most frequently called for in joint affections.

*Pressure* with the palm or finger tips is also conceded a part of every systematic massage, chiefly applicable to nerves and vessels.

*Vibration* is an oscillatory motion imparted to the extremities by grasping the hand or foot and, by short jerky motions, causing the member to sway. A shivery action of the palm or fingers is a convenient way of applying vibration to the internal organs.

*Stroking,* as the last manipulation, is a modified form of pressure. It is executed by making long sweeping strokes with pressure.

John Mitchell is the principal authority on mechanotherapy in the United States and has written largely on the subject. He classifies the methods of massage in a somewhat different manner to those given above, and states that massage movements are of four classes to which are attached French names, namely: 1, Effleurage; 2, Pétrissage; 3, Friction, and 4, Tapotement.

Effleurage is slow stroking with the flat hand, the heel of the hand, the edge of the hand, a thumb, thumb and fingers, or finger tips. Effleurage is used as an introductory movement to begin the manipulations, either with one hand, with both together or alternating. Its physiological effect is the hurrying of venous and lymphatic currents.

Pétrissage is performed by grasping with the whole hand the tissues to be operated upon, lifting a little the mass thus seized and kneading it with an alternate tightening and loosening of the hold. This is the most important movement of massage, and requires a considerable degree of skill to be properly used. There are several forms or modifications of this form of manipulation—rolling, fist kneading, wringing, pulling and push rolling. The general effects of pétrissage are a slight, direct stimulation of the muscles, a hurrying of the lymphatic and venous circulation, and thus an indirect effect upon the arterial stream, great increase in the quantity of blood flowing through the tissues manipulated, and more remotely an actual increase in the number of blood cells.

Tapotement may be defined in its different forms as a series of rapid blows delivered with the finger tips—percussion; the flat of the hand—slapping; the edge of the hand—hacking; or by means of vibratory movements made by the hand—vibration.

Graham referring to the mode of applying massage does not agree with the appositeness of the terms, effleurage, pétrissage, etc., but thinks that these and other subdivisions should be grouped under four heads: Friction, percussion, movement and manipulation. Malaxation, deep rubbing or kneading, is a combination of pressure and movement, without allowing the hand to slip on the skin.

Concerning the technic of massage Mitchell says, if a merely local condition is to be treated,—as a sprain, a luxation or a deposit

of inflammatory exudate,—short and frequent applications should be used. General massage of the whole body as a means of combatting the ill effects of enforced inactivity, in convalescence as a promoter of nutrition, or as introductory to more energetic exercise should be given at least once daily, and in bed-fast patients—for example, during the rest treatment—may sometimes be used twice a day with advantage. In disorders wholly local, frequent short applications are best,—for example, from five to fifteen minutes, twice, thrice or four times daily. In extreme old age, in arthritic diseases with adhesions, the patient is sometimes unable to endure the pain of effectual manipulation more than once in two or three days. When continuing efforts are wanted as in promoting absorption of exudates, or stimulating circulation in weak or palsied parts, long treatment is ordered; but how long must depend upon the extent of territory involved, and on the masseur's observations of the result of manipulation. A single limb may be rubbed from eight to fifteen minutes; if only a part of the limb is treated, the time must be reduced. General massage in convalescence, in rest treatment, in anæmia and similar conditions, should last from fifty to sixty minutes; or in large and fat people even seventy-five minutes.

The general effects of massage are said to render muscles firmer and to stimulate the secretion of the skin. The ordinary physiological effects of mixed massage are a temporary increase of temperature and a slowing and strengthening of the pulse. Physiological effects of massage are somewhat as follows:

It exerts an influence upon all the superficial tissues. It renders the skin softer and more supple, but at the same time tough, flexible and elastic. It acts on the muscles in a correspondingly beneficial manner. Its effect on the blood and lymphatic circulation is to increase the flow. Deep, slow kneading is the most effective and necessary form. It is claimed that by this mode of massage the deep as well as the superficial circulation is changed and in a short time a great addition to the actual number of red blood cells in the vessels is brought about. The hæmoglobin value of the blood corpuscles is somewhat increased. The lymphatic stream is hastened. There is a larger secretion of urine containing an added proportion of solids. The nerves are excited in all their functions.

The influence of massage upon the pathological processes is also very considerable. There is the danger from massage of forcing into the circulation, or releasing from foci, pathogenic bacteria which may, because of an enfeebled resistance, overwhelm the army of defense and light up an old complaint or start systemic conditions where the germ was formerly quiescent.

*Indications.*—Massage is of service to the human economy in health and disease, but the acute stage of any illness constitutes an invariable contraindication to its use. A general massage is of prime service in neurasthenia and those run-down conditions (asthenia) which are an accompaniment or a consequence of systemic disorders and protracted illness. Otherwise its application is generally local, to aid in the dispersion and absorption of extravasated fluids, *i.e.,* ecchymosis hæmatoma and œdema, whatever its origin. The blood that is spilled into the tissues with sprains and into the joints and between the bone-fragments in fractures is greatly hastened in its absorption by massage immediately following the injury and conducted in a very gentle manner at first, and with increased vigor as time progresses, but always short of pain. The massage should, in fractures and joint injuries, be directed towards the muscles also, to prevent their atrophy during the interim of healing.

Muscles paralyzed because of injury to peripheral nerves may be massaged and prevented from atrophying in a great degree while the nerve is being restored. Where the paralysis is of central origin, affecting the nutrient (trophic) centres, massage is of little avail as far as benefit to muscles is concerned, but errors in circulation, œdema and cyanosis, may be overcome.

For the cure of chronic constipation, the abdominal muscles should be massaged with the various motions, and then the coils of intestines should be subjected to kneading and pressure.

After subsidence of the acute manifestations of pelvic peritonitis and pelvic cellulitis, a massage of the uterus, after the fashion of a bimanual examination, will greatly facilitate the absorption of the intrapelvic exudate.

With a finger in the rectum, massage can be given to a chronically affected prostate and the seminal vesicles. The pathological content of each organ is thus emptied into the bladder, there to be

expelled with the urine. Both uterine and prostatic massage are to be supplemented by massage of perineal, lumbar, and hypogastric regions.

These constitute the main indications for massage, which can always be enlarged upon whatever the tone of the muscle and the circulation can be improved.

*Whooping-cough treated by Manipulation of the Lower Jaw.*—Naegeli, speaking from a personal experience, and from the treatment of his two children with pertussis, says that the spasm of the glottis is like that occurring in asphyxia of chloroform narcosis, is due to spasm of the cricothyroid muscles, and can be overcome by pulling the lower jaw forcibly downward and forward with the flexed index finger behind the ascending rami. Naegeli tried the method at least 500 times with brilliant results.

*Swedish Movements* (resistance movement).—These movements are executed by having the patient overcome (active) the effort of the masseur to execute certain passive counter motions of the various members of the body. Thus if the patient flex the forearm his effort to maintain this position against the masseur's endeavor to extend the forearm constitutes a resistance movement. Again, the attempt of the patient to expand the thorax against the counter pressure of the masseur's hand on the chest is another instance, and so examples might be multiplied. These efforts of the patient constitute the so-called active phase of Swedish movements. The passive type implies entire relaxation of the muscles, the whole cycle of motions of any joint being executed by the masseur. A combination of these motions with or without hydrotherapy find their most extensive and useful application in the familiar medical gymnastics for valvular and functional heart affections.

This treatment is to be supplementary to all other forms of cardiotherapy and should be very gently conducted—as a special part of massage of the entire body. Its effects on the heart must be carefully watched. A seance of ten minutes is sufficient at the outset.

Joints stiffened by disease or injury are also markedly benefitted by Swedish movements. All of these various forms of motion can be executed in a very mechanical way by aid of specially constructed machinery devised by Zander. With these ingenious devices the

degree of force applied can in each instance be accurately gauged. Institutes abound in most European centres and in New York for this treatment.

Massage in one form or another is indicated in hysteria, neurasthenia and in drug habituations. In the system paralyses due to nutritive changes or degenerative alteration of the spinal cord, the results of massage vary according to the cause of the disorder, its extent and especially the stage at which treatment is begun.

According to the present methods of treating locomotor ataxia exercise afoot is prohibited; thus massage is a useful agent in promoting circulation, as well as favoring physical condition. Massage is also said to be of some value in infantile spastic paralysis and is frequently of avail in insomnia.

The malnutrition which accompanies certain forms of insanity has been successfully treated by massage. The method is also considered to be of use as an adjunct treatment in some of the forms of heart disease, although massage of the heart itself is not to be recommended.

Hydrotherapy combined with massage is stated by some authorities to have given good results in functional disorders of the heart and circulation. Massage is generally used in obesity and is undoubtedly in many cases of this condition a valuable contributory means of treatment. It is also indicated in muscular rheumatism, sciatica and other neuralgias, in some forms of headache, in local congestions and in inflammatory affections of the eye. Disorders of the digestive organs frequently yield to massage.

Little can be definitely stated with regard to the effect of massage upon the nervous system. It would appear in the light of experience that nervous affections of a functional and peripheral origin offer the most favorable opportunities for this method of treatment, but in such cases even, it would be unwise to make a certain prognosis.

The treatment of fractures, dislocations, and sprains by means of mechanotherapy was first advocated by Lucas-Championnière and the method has been applied with some success in France and in Europe.

Torticollis arising from cold or rheumatism has been often completely cured in a day or two by massage. Spasmodic torticollis has

also shown itself to be to a certain extent amenable to similar treatment.

Thure-Brandt originated uterine massage and it has been advocated by Propanter, Prochovnik and Schanta. This form of massage is well-known throughout Europe, but has gained little headway in America.

Massage of the breasts with the object of inducing a flow of milk or of increasing deficient secretion has been employed with good results. Cosmetic massage is now so largely exploited by barbers and beauty doctors, that it has fallen somewhat into disrepute with the medical profession. However, when properly employed it has been found useful in the treatment of blemishes of the skin.

Before leaving the subject it might be appropriate to give Weir Mitchell's plan in the treatment of obstinate sciaticas of neuralgic or nuritic origin. To lessen the blood in the limb, and to remove the irritation caused by motion, the patient is confined to bed, the leg bandaged firmly from the toes to the groin with a flannel bandage, and the hip and knee joints fixed by a long splint from axilla to ankle, or, in patients who can be trusted to keep quiet, by sandbags. The bandage is removed and the leg rubbed twice daily, general kneading of the muscles being employed, except of those near the nerve; even indirect pressure upon that structure is to be avoided.

The nerve tract is to be "effleuried" with long steady strokes; the hip and knee joints passively flexed once or twice in a gentle manner, and the bandage reapplied. It is stated that three weeks of this procedure will usually suffice for a cure even in obstinate cases.

The great value of massage in cases of drug habituation and alcoholism should be given special emphasis. It should be administered throughout the course of treatment and very carefully during the collapse, which is the invariable sequence of the final withdrawal of the accustomed drug. The weak condition of the heart in such patients demands assistance, especially in those addicted to morphia. Further, as the stomach is usually deranged and irritable, such a means of strengthening the blood circulation, without at the same time upsetting the stomach, is an advantage.

It has, too, a strong sedative action, partly due to the relaxation of the peripheral vessels and partly to the soothing influence it exerts over the unstrung nerves.

In recapitulation it may be said of general massage, that it tends to strengthen weak muscles, to stimulate the action of the skin, to promote digestion and to increase the movements of the intestines. It is of great assistance to a feeble circulation, and will relieve an overworked heart. Its influence is great upon the blood-making functions, and for this reason is of special service in cases of anæmia. Increased diuresis is caused by its action upon blood vessels.

According to Mitchell the contraindications to general massage are fevers, breaks in the skin, pus formations, malignant growths and cystic tumors. Contraindications to local massage—acute inflammatory conditions local or general, periosteal or peritoneal.

Patients with gastric or duodenal ulcers should not be rubbed, nor should massage be employed in cases of atheroma, aneurism, and severe varicose veins, nor wherever and whenever there is any marked tendency to or any sign of serious weakness of the blood vessel walls.

*Manual Vibratory Stimulation.*—Vibration possesses the same remedial virtues as percussion and is, in certain conditions, more valuable perhaps than any of the other methods of treatment which have been discussed in this paper. In the stimulation of deep lying muscles, it is strongly indicated; this is especially true in those of the intestines.

By some physicians it is recommended in the treatment of neuralgias, and it is stated, in certain cases of this affection, to have been of great benefit. Vibration is occasionally used in general treatment by means of the shaking chair invented by Charcot. In habitual constipation, characterized by a lack of biliary secretion, vibration in the vicinity of the liver and the gall duct has been employed with success. In cases of atony of the rectum, or of impaired action of the ileocæcal valve, vibratory movements are usually found of service.

For the former condition the modus operandi is thus described by Mitchell. The fingers held pyramidally together are pressed deeply down in the left iliac fossa, so as to approach as near the head

of the rectum as is possible, and strong vibratory movements are then imparted to the hand by contracting the forearm muscles. To stimulate the relaxation of the ileocæcal valve and allow the propulsion of intestinal contents from the small into the large intestine, a similar movement should be administered at the point of juncture of these two portions of the intestine. Vibration applied directly to the anal orifice is said to have a stimulating effect on rectal contraction.

It is stated that vibration given at the ileocæcal junction and also about the head of the rectum, if well done, will frequently produce an evacuation of the bowels within a few minutes.

Old arthritic adhesions are perhaps most effectually treated by first using vibratory movements in order to promote the circulation, and afterwards by means of apparatus, steady, slow, increased passive movements. Vibration has been recommended in the treatment of migraine, but many nervous patients cannot endure the manipulation during an attack.

Charcot had a very high opinion of the value of vibration in the treatment of paralysis agitans, and for this purpose used the shaking chair, as well as local vibrations, manual and mechanical.

Ocular massage or vibration is used in the treatment of a large number of eye effections, but its use is contraindicated in others. It should not be used in acute inflammations of the conjunctiva, cornea, sclera, iris and ciliary body, or after accidents. It should be borne in mind that in the treatment of the eye, mechanical methods are not without danger.

Eye massage can be effected by the fingers or by apparatus. The electric vibrator of Maklakow is a good example of mechanical means. By this instrument tapotement is effected by a small hammer striking on the eyeball, with short, regular vibrations, if necessary as rapidly as 9,000 in a minute.

Oscillators are also made by which rarefaction of air causes a forward and backward movement of the eye.

As to the comparative beneficial effects of manual and mechanical vibration, opinions differ. Certain effects can be produced by mechanical means which cannot be produced by the best manual treatment.

On the other hand, machinery cannot be altered when it has once been started but must continue at the same uniform speed until its work upon a patient is completed. The enormous cost of a mechanical outfit and of its running is against its general employment.

# CURABILITY OF TUBERCULOSIS

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As time passes and experience aids me in drawing conclusions somewhat independently of my confreres, I am frank to say, that a great deal of nonsense has been written and expressed about the curability of tuberculosis. I have reference particularly to the pulmonary type of this disease. The human race has been afflicted with consumption for thousands of years, and for thousands of years people have been dying of it. No "cure" has been discovered that I am aware of, and yet we have hastily removed tuberculosis from the list of incurable diseases and classed it as curable. We doctors have some failings, and the chase for a will o' the wisp is often one of them. In this matter as in others the truth is more likely found in the mean than the extreme, and my friend, Doctor Musser, is perfectly right when he says "tuberculosis is sometimes curable."

A peculiar mental state, an obsession, so to speak, often seems to dominate special workers. We cannot but view with sympathy the flounderings of the human intellect in the task of wresting facts from nature. It is a Titanic struggle at times, and almost too much for the mind of man, and yet what has been accomplished gives encouragement to continue. It is, however, sometimes a healthy thing to stop and see just where we are; to leave the laboratory, the study, and our patients, and go outside where perchance the contemplation of space will help us to understand that, so far, we have but scratched the surface of things in this world. It is indeed humiliating to make a positive statement, and then, a little later, have the whole position to reconsider; and yet in this unceasing struggle with God's infinities we should have a broad sympathy with the mind that goes astray in the search for truth. It is apparently easier for lesser minds to keep sane than for greater ones to do so. Our very limitations are our safe-

guards, and it thus becomes a duty to apply our broader vision to this problem, curability of tuberculosis.

To return to our specialist with an obsession, Von Behring has his "tulase," and some nearer home, waxing enthusiastic, proclaim to an audience of laymen, "sixty per cent. of our patients are practically cured." What can practically cured mean? Certainly not cured, for why the qualifying practically? All this with no deliberate attempt to deceive, the result rather of an almost childish enthusiasm, the stress of the moment, and sometimes, I regret to say, an attempt to place things in the most favorable light in order to squeeze money for a good cause from a reluctant legislature. It is a jesuitical type of reasoning that in the end will merit and receive disaster. In sober sense the truth is what we most desire and sooner or later must have. I would like to make my contribution to this truth with the statement that I do not consider tuberculosis a curable disease, but only that it is sometimes curable under propitious circumstances, trusting that in what follows I will be able to furnish the justification for my belief.

I am almost daily struck with the fact that my patients upon presenting themselves for treatment, and quite regardless of the stage of the disease, tell me, nearly without exception, that they have been assured that they will get well, and therefore expect a cure at my hands. This shows how this curability fallacy has permeated our profession, for you cannot persuade me that these people have been consciously lied to. About the first duty I have to perform is the very disagreeable one of destroying a comforting illusion, and changing the whole point of view in regard to the disease; for I hold that a clear conception on the part of our patients is almost essential if any good is to be accomplished for them. Deception has no place in medical practice. We have a right to all the truth, little enough to be sure, that we can lay hold of, and so have those to whom we minister. My first duty, therefore, is to re-educate my patients, and tell them that in no case can we assure a cure; that, in fact, the result is altogether problematic. If tuberculosis is a curable disease it would follow that occasionally at least we would be justified in assuring a patient of a good result. They have been told "go down to New Mexico to

Doctor —— and he will fix you up in a few months." No such potency is possessed by physicians, and after years of this work I am frank to say that the result is often a disappointment to all concerned. In a case in which I am naturally led to expect recovery the patient goes straight on to death, and in others, much more unfavorable, astounding recoveries occur. Twenty-five years ago no one recovered from consumption, and now everybody gets well.

A good many years ago when I came West in search of health, my medical friends felt very sceptical as to the result. I could realize this by the attempt to conceal a sympathetic tone in discussing it with me. Now all this is changed, and under similar conditions I would be told, "of course you will get well!" Nothing of sufficient importance in the treatment of tuberculosis has been discovered to justify this entirely changed attitude toward the disease. The time has come to retrace our steps a little way. I had an insignificant lesion myself, insignificant as such things can be, and yet at the end of six months I had just succeeded in ridding myself of fever, and it required two years altogether for me to get on my feet. Still patients with enormous lesions are told, "you will be all right in six months!" Dr. Trudeau and I, and every other man who for years has been engaged in a hand to hand struggle with this still awful disease, know better, especially if we have kept clear of obsessions, and attempts to make financial successes of the work. As an invalid in a Colorado resort I heard all sorts of talk about cure, but I saw little of it; so little in fact, that it was pity for the wandering "lunger" and not "cure" that originally took me into the work.

My labors in the field of tuberculosis have all been in "closed institutions" in one of the most perfect climates in the world, and so, if I have taken advantage of my opportunities, my results should be as good as any, and, as a matter of fact, I am quite sure they are. Our potential armamentarium in tuberculosis is very limited, and within the reach of all. There are certain general principles to which we are tied hand and foot. Our efficiency as a specialist in this disease depends upon our influence over our patients rather than upon prescription writing. Thus, we are all

placed very much upon equality when it comes to getting results, and this should, I think, make us very sceptical of reported results that are much better than the average obtained under similar conditions.

Some people do get well of tuberculosis. Now who are they? (I myself am an example of perfect cure for at least ten years to my certain knowledge.) The reply to this question is easy. Principally incipient cases recover, because the lesion is small and resistance not yet broken; and, let me emphasize, human nature and finances are strong enough to stand the comparatively short period, nine months to a year, that is necessary to obtain the result. If the recovery is longer delayed, one or both of these factors, weak human nature or lack of means, will often block further progress towards health. When this time arrives, and we physicians are forced to release the patient, what are the results? Sixty to seventy per cent. of these incipient cases have apparently recovered. We have, of course, remaining in almost every case the physical signs of condensation over the former lesion. Of the remaining thirty to forty per cent. the greater portion are better. In some, that "arrest" which is often illusive, has occurred. Some improve to a certain point, and then "stick in the mud," as the saying goes. A few, a very few, take on gradually the characteristics of progression. Practically none of this class ever die under treatment.

Up to the present time we have sent out sixty to seventy per cent. apparently cured, and of these about twenty per cent. eventually relapse. So even in our most favorable class, the incipients, under the most favorable conditions, sanatorium life in a beautiful climate, the real cures are reduced to from forty to fifty per cent. My observation is that the others of this class, those discharged improved, unimproved and arrested, ultimately die of the disease. As we see tuberculosis in the West incipient cases compose less than twenty-five per cent. of the total number presenting for treatment, and therefore in my experience at least, real cures are comparatively infrequent, and a small minority of the total number of tuberculous men and women who pass through my hands recover. Some of the relapses that occur in this most favorable class which we have been considering are preventable, the result of carelessness

maybe, but most of them are the result purely and simply of the inexorable exigencies of life. With tuberculin we can save some of the incipients who otherwise would be discharged as improved, or unimproved, or possibly arrested, but not many; and tuberculin administration is a time consuming procedure requiring much patience from both doctor and invalid. As might be expected, a larger number of my cures relapse among those who return East than among those who remain West. This is proof positive to my mind that these people should remain in the climatic and social environment in which recovery occurs.

Among a certain school of phthisiotherapists it has been the fashion during the past few years to malign climate in the treatment of tuberculosis. This does not effect the everlasting truth that even without treatment consumptives live longer in high dry climates than in low humid regions, and that, quite unaided, a larger percentage eventually recover when in dry climates than under similar conditions at home. In this matter of climate all we have to do is to await patiently the return swing of the pendulum, of which there are portents even now.

To return for a moment to our incipient cases and their fate, one fact stands forth prominently: With thirty to forty per cent. of relative, if not complete failures in the most favorable class, it is certainly wrong, almost a crime, to assure anyone of a recovery. I feel satisfied in telling my patients with incipient lesions that they have about seventy per cent. of chances in their favor, provided they are good, conscientious patients, and can give up enough time to the business of getting well.

Outside my own work, which as before mentioned, has been under the very favorable conditions of institutional life, I have been intensely interested in observing what happens to the invalids in an open resort like Silver City, a place that climatically is all that can be desired. First, I should explain that incipient cases are comparatively rare among the unattached health-seekers found there. Most of the cases are moderately and far advanced. Very few cures are known to have occurred. It is a fact that at a recent meeting of the County Medical Society we succeeded in counting about a dozen cures, actual cures, in a period of eight years occurring in the town itself, exclusive of the various sanatoria located

there. This does not speak very highly for the open method of treatment, and bears out already observed experience that actual cure is mostly a question of institutional management. It really required hundreds of cases to furnish these twelve cures. It proves that the pulmonary invalid East or West is much better off in an institution arranged for his benefit.

Side by side with the fact that few cures are obtained in Silver City, should be placed the fact, which is even more important, that few of the consumptives who reside there, mostly advanced and far advanced cases, really die of the disease, or if they do, only after years of usefulness in spite of the morning cough. The work of the town is to a certain extent done by them. Year after year they live and do this work. Occasionally they are laid up for repairs, of course, but most of the time they get along without help, medical or otherwise, surprisingly well. Sometimes one of their number drops off, for I do not mean to imply that they live forever, but to one who has worked among the phthisical in the East the way these patients live in the West is really astounding. I have attended a meeting of the medical men of the Territory when not over two or three of the members present possessed healthy lungs, and to observe them one would not imagine that they were afflicted with a serious disease or had been so afflicted in the past. Even among our unattached, untreated invalids diarrhœas, night-sweats, and hæmorrhages are very very rare. In refering to the type of invalid who does as well as this, I am excluding phthisis florida, as might be taken for granted, and have reference particularly to the chronic cases which are principally of the afebrile class All this help which these patients receive we, who really know, who have lived and worked among consumptives both East and West, are ready and willing to attribute to the much abused climate. That is why, after years of careful observation, I am still the tireless apostle of the doctrine: "For God's sake don't go home!"

We have discussed at some length what becomes of the incipient cases treated in an institution in a favorable climate. Now what becomes of the seventy-five per cent. of all our cases who make up the advanced and far advanced classes. Untreated, in this climate, we have already indicated their destiny. But now I am discussing the institutional cases of this class. Many of them, poor unfortu-

nates, are sometime incipients who have reached a more advanced stage while taking the cure at home. As time goes on and for various reasons I lose faith in the curability of tuberculosis, principally on account of the advanced class we receive, while I gain faith in the improvability of the disease, for the very simple reason that most of the patients I consent to keep longer than a month do actually improve, almost or quite to the point of complete restoration of general health. In this connection it must be remembered that we are discussing moderately advanced and far advanced cases. If this improvement can only be maintained long enough a permanent good result should follow, and usually does in those exceptional instances in which temperament, character, and finances all combine to contribute each its share towards the final accomplishment of a good result. I can go through my protocols and find marvelous results where this fortuitous combination has existed. Cases, in fact, I would be inclined to discredit if someone else told me of them. But instances like this are so rare in institutional work, that from the point of view of cure in the more advanced classes, they are reduced to a negligible quantity as far as practical results are concerned.

In my experience we can obtain, in the time alloted to us, twenty per cent. of apparent cures in moderately advanced cases, and in the far advanced class the apparent cures fall to eleven per cent. As I tabulate my cases I can see particularly in these results the operation of the factors before mentioned, namely, temperament, character, time, or what is about the same thing, money, in fortuitous combination.

It simply resolves itself into this: Not so much on account of the inherent incurability of the disease though that plays its part, but on account of the time involved in the gradual involution of an extensive lesion, cure in moderately advanced and far advanced tuberculosis is usually unattainable. The small percentage which we do save and eventually class as apparent cures is insignificant when placed beside the list of failures. Not long ago a prominent specialist in one of our health resort cities published with much pride a list of twelve or fourteen hopeless cases which were seemingly improved under treatment. I wonder if any man in the work could not do the same thing? To make the position clear,

however, the same specialist should have published a list of his failures in the same class. I suppose hundreds of poor unfortunates have since crossed the continent on the strength of those twelve or fourteen cases and probably most of them are dead.

The average time which my patients remain in the sanatorium is about seven months. What in the way of permanent results can I be expected to obtain in these advanced classes in seven months? Here is a lesion years old and I am expected to see it disappear in seven months. Yet both home doctor and patient unite in expecting these wonders to come true. I do not get such cures. Patients which are considered as the most favorable subjects in the class we have been discussing, are improved in general condition at the time of discharge, and this is all that ought to be expected. The end result will depend, to a certain extent, upon where and how they live, but in most of them continued improvement after leaving the institution is incompatible with the life they are forced to lead. Under favorable conditions they have been able to improve when actually in a very serious state. Under the stress of life, as it is forced upon them, I do not think that it is natural or reasonable to suppose that this improvement will continue. Most patients discharged as improved or arrested sooner or later must die of the disease; sooner if they have at all a hard time or are forced to work with their muscles or indoors, and later if conditions are such as to make possible a relative degree of good care. Later also, if they remain in the environment where relative recovery has occurred. In this class of advanced cases we have seen that it is possible to obtain a small number of cures, a larger percentage of improvements, and some arrests. We have left, however, about fifty per cent. that should be classed as unqualified failures, all of whom are doomed to death in a short time.

To sum up: A very large proportion of the incipient cases under good conditions in a good climate do really recover. In about twenty per cent. of these, relapses occur later, and, after all, the cure is but an apparent one. Under similar conditions about fifty per cent. of those further advanced, and these still compose the vast majority of our patients, show unqualified improvement, and in most of these the degree of improvement and its

permanency are in direct relation to the length of time they will or can give up to the business of getting better.

For the sake of clearness it may be well to repeat: Under conditions of life as we know them, it is perfectly safe to say tuberculosis is but sometimes curable.

Trudeau has shown that by the careful use of tuberculin we can improve our results a little, and what is more important, make them more durable; but the influence of tuberculin is not so marked as to invalidate in any way the opinion expressed above. Practically then, the curable cases are the incipient cases. Curability depends almost entirely upon incipiency, and therefore, if we would change the still gloomy picture presented by tuberculosis, we must teach and inculcate early diagnosis, which in spite of all that has been written and expressed on the subject is still almost an unbroken field. We who daily work with tuberculosis and take histories as a matter of constant routine know this very well. A patient with clearly demonstrable lesion is told time after time "nothing is the matter" or treated for something else. Sceptical, he seeks more skilled opinion, or what he supposes to be such, and finally, after incurable damage has occurred the diagnosis is made.

With such a deplorable condition still so common it cannot be amiss to go over once more the points of early diagnosis. If the diagnosis of an internal disease is in doubt tuberculosis should be excluded positively before going further. Since it is the most common of all diseases, the medical mind should be trained to demonstrate its presence; always to be on the alert. From my experience it seems plain that in this country the average practitioner does not recognize the presence of tuberculosis much earlier than the patient and his friends do. Auscultation through the clothing is a piece of carelessness only mentioned to be condemned. It is impossible to demonstrate a very early lesion of an apex with the unaided ear. A negative pulmonary examination by an expert does not exclude tuberculosis, the disease often being months old before the most carefully trained ear can demonstrate its presence. It may exist in the bronchial glands for years before reaching the lungs. Bacilli in the sputum, or, in fact, any sputum at all, is a comparatively late sign. Percussion is practically valueless in very early stages. The same is true of voice and whisper

transmission. Nothing but auscultation of breath sounds should be depended upon in this stage. Other signs are helpful when present but mean nothing when absent. A patient should never be reassured upon the occurrence of a hæmorrhage from the respiratory tract, or told, off hand, that it is from his throat. A hæmorrhage is often a rather early sign and therefore helpful in diagnosis, especially as it is often the first thing that calls the patient's attention to himself, and thus brings him under medical observation. I remember a case in point many years ago. A patient of mine had a slight hæmorrhage, and unable to make a diagnosis from the physical findings I took him to an eminent specialist in New York, who assured him, and therefore me, that nothing was the matter. Eight years later my patient died of tuberculosis, remaining free from other signs for six years after the hæmorrhage. Nature's red flag, as a hæmorrhage has been called, should never be overlooked or underestimated.

In the tuberculin test we have practically an unequivocal method of diagnosis in the earliest stages, and one that the broadest experience, that of Dr. Trudeau, shows when correctly applied, to be perfectly safe. It is therefore almost criminal to neglect any opportunity of applying this test. Every physician should understand its application, and should employ it even oftener than urinary analysis.

With our present methods of treatment there is but one way open to enable us to exclude tuberculosis from the list of incurable diseases, and that is to get the tuberculous patient under observation and treatment in the very earliest stages of the disease. Early diagnosis is the only way to accomplish this result. To show in a word how important this is, let me state most earnestly that in all my experience, embracing about fifteen hundred cases of tuberculosis in all stages, I have not a single failure to record in the so-called closed cases, before ulceration has occurred.

# Medicine

## THE BLOOD PRESSURE IN TUBERCULOSIS *

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The observations recorded in this paper were, with few exceptions, made upon the patients in the Tuberculosis Department of the Philadelphia Hospital. They represent a part of a study made during the past year upon the Circulation in Tuberculosis. The work was done under my direction by Messrs. H. L. Hull and E. C. Sherrick of the Research class of the Jefferson Medical College. The urine examinations were made under the direction of Dr. A. G. Ellis. The eye examinations in the nephritic cases were made by Dr. George E. de Schweinitz to whom I wish to express my sincere thanks.

The circulatory phenomena in tuberculosis are of extreme importance in prognosis and treatment, and to a less degree in diagnosis. While this communication deals solely with the blood pressure, the pressure estimations are to be considered only as a part of the general examination. Several observers—notably Burckhardt, Nauman, and Igerscheimer—have published investigations upon the blood pressure in pulmonary tuberculosis. Nearly all of these investigators have tried to show the effect of tuberculosis *per se* upon the blood pressure, and accordingly they tried to eliminate all cases showing complications such as nephritis, arteriosclerosis and the like. To know the exact effect of tuberculosis upon the blood pressure would be of great interest, but practically this is not possible as most of the cases are complicated, and kidney involvement, the most potent factor in influencing blood pressure, is frequently

* Read before the Pathological Society of Philadelphia, 1907.

met with. Besides this the effect of previous infections must be considered when studying the present blood pressure of any individual. Thus Thayer has pointed out that individuals who have had typhoid fever will show a disproportionately higher pressure later on in life. It is quite possible that other infections, as pneumonia and diphtheria, might have a like after effect. The same applies to gonorrhœa and especially to syphilis. Finally the possible influence of alcohol must be considered. This is of particular interest, as it has long had the reputation of curing tuberculosis. It also has been credited with producing arteriosclerosis, and its beneficial effects may have been due to its action on the blood pressure.

Since the tuberculosis patient may have been subject to all the above influences prior to his outbreak of phthisis, these factors have all been studied along with the blood pressure. Likewise we have noted age, sex, temperature, pulse rate standing and lying, presence of cardiac murmurs and accentuations and arteriosclerosis. Unfortunately it was impossible to secure data as to height and weight.

### METHOD OF OBSERVATION

It is, of course, natural that for these estimations my own Indicator, a modification of the Rivo Rocci instrument, was used. The estimation of the systolic pressure by palpation of the pulse is to my mind the easiest and most accurate criterion so far found. Almost any two observers will get the same results on the same patient. The determination of the diastolic pressure by observing the point of greatest oscillation is slightly harder, but the ability is soon acquired. The particular form of Riva Rocci used is a matter of personal taste. The Gärtner "Tonometer" I unhesitatingly condemn after a most thorough trial. The discrepancies in the findings of Burckhardt and Igerscheimer show its range of error and its many shortcomings have already been pointed out in a paper on the circulation in pregnancy by Dr. Stengel and myself. The present series of estimations were made with the Indicator, using a 10 c.m. cuff. All pressures were taken from the left arm with the patient stripped to the waist and in a recumbent position. As the first estimation is nearly always too high, the estimation was repeated until a level was obtained. Our data on blood

pressure include the systolic pressure; the diastolic pressure; the pulse pressure, which is the difference between the systolic and diastolic pressures; and the mean pressure, which is calculated by adding to the diastolic pressure one-third of the pulse pressure.

These patients were all living under the same conditions as to diet and hygiene. The possible influence of drugs was eliminated, as the only medication employed was a preparation containing a small amount of nux vomica—too small to be of moment.

The total number of cases was two hundred and twenty-two, of which one hundred and ninety-seven were white and twenty-five were black.

### SEX AND BLOOD PRESSURE

There were one hundred and sixty males and fifty-one females. The sex was not noted in one case.

| Number of Male Cases, 160 | | Number of Female Cases, 51. | |
|---|---|---|---|
| Average Systolic Pressure | 103.7 | Average Systolic Pressure | 99.4 |
| Average Diastolic Pressure | 77.4 | Average Diastolic Pressure | 76.7 |
| Average Pulse Pressure | 26.3 | Average Pulse Pressure | 22.7 |
| Average Mean Pressure | 85.11 | Average Mean Pressure | 84.22 |

These results are in accord with the usual findings, that the systolic blood pressure in women is lower than in man. The difference in the diastolic pressure is surprisingly small. It suggests that in the human species the lowest limit at which the functions of the body can be carried on is very nearly the same in every individual, while strength and the ability to perform work is a matter of systolic pressure. The pulse pressure in the male is accordingly higher than in the female.

### TIME OF DAY AND BLOOD PRESSURE

| A.M. | | P.M. | |
|---|---|---|---|
| Male Cases, 70. | | Male Cases, 98. | |
| Average Systolic Pressure | 104.06 | Average Systolic Pressure | 106.59 |
| Average Diastolic Pressure | 78.57 | Average Diastolic Pressure | 76.89 |
| Average Pulse Pressure | 25.49 | Average Pulse Pressure | 30.3 |
| Average Mean Pressure | 87.06 | Average Mean Pressure | 86.9 |

Apparently this would show a higher systolic and a lower diastolic pressure in the afternoon, thus increasing the pulse pressure. The female cases, however, show the opposite condition.

| A.M. | | P.M. | |
|---|---|---|---|
| Female Cases, 26. | | Female Cases, 25. | |
| Average Systolic Pressure | 100.84 | Average Systolic Pressure | 97.88 |
| Average Diastolic Pressure | 76.11 | Average Diastolic Pressure | 76.36 |
| Average Pulse Pressure | 24.73 | Average Pulse Pressure | 21.52 |
| Average Mean Pressure | 84.33 | Average Mean Pressure | 83.53 |

The behavior of the mean pressure in both groups is practically identical. It is apparent that whatever the conditions may be the organism strives to maintain this mean.

With the idea of determining whether there was a regular variation at different hours in the day, a series of twenty cases were taken and the pressure estimated five times daily. Ten of these cases had fever, and ten were non-febrile. No definite change could be detected. There were variations in the blood pressure, but this apparently had nothing to do with the time of day.

*Blood Pressure and Age.*—For the sake of accurate comparison the cases were divided into ten groups as follows: Under 15 years; 15 to 20 years; then at 5-year periods up to 50 years; 50 to 60 years; 60 years and over.

| Group I. | No. of Cases 3. | | Ages—Under 15 yrs. |
|---|---|---|---|
| Average Systolic Pressure | 90.67 | Highest 95 | Lowest 87 |
| Average Diastolic Pressure | 69.33 | Highest 75 | Lowest 65 |
| Average Pulse Pressure | 21.33 | | |
| Average Mean Pressure | 76.44 | | |
| Average Pulse rate standing | 119.33 | Highest 136 | Lowest 110 |
| Average Pulse rate recumbent | 105.33 | Highest 116 | Lowest 94 |

| Group II. | No. of Cases 3. | | Ages—15 to 20 yrs. |
|---|---|---|---|
| Average Systolic Pressure | 100.33 | Highest 120 | Lowest 86 |
| Average Diastolic Pressure | 74.33 | Highest 90 | Lowest 65 |
| Average Pulse Pressure | 26 | | |
| Average Mean Pressure | 83 | | |
| Average Pulse Rate standing | 112.67 | Highest 135 | Lowest 85 |
| Average Pulse Rate recumbent | 107 | Highest 120 | Lowest 85 |

| Group III. | No. of Cases 15. | | Ages—20 to 25 yrs. |
|---|---|---|---|
| Average Systolic Pressure | 99.33 | Highest 122 | Lowest 75 |
| Average Diastolic Pressure | 73.20 | Highest 95 | Lowest 58 |
| Average Pulse Pressure | 26.13 | | |
| Average Mean Pressure | 81.91 | | |
| Average Pulse Rate standing | 116.35 | Highest 138 | Lowest 80 |
| Average Pulse Rate recumbent | 104.20 | Highest 120 | Lowest 70 |

| Group IV. | No. of Cases 16. | | Ages—25 to 30 yrs. |
|---|---|---|---|
| Average Systolic Pressure | 103.43 | Highest 125 | Lowest 75 |
| Average Diastolic Pressure | 75.87 | Highest 90 | Lowest 58 |
| Average Pulse Pressure | 27.56 | | |
| Average Mean Pressure | 85.06 | | |
| Average Pulse Rate standing | 113.20 | Highest 142 | Lowest 86 |
| Average Pulse Rate recumbent | 99.62 | Highest 130 | Lowest 70 |

| Group V. | No. of Cases 28. | | Ages—30 to 35 yrs. |
|---|---|---|---|
| Average Systolic Pressure | 90.25 | Highest 120 | Lowest 80 |
| Average Diastolic Pressure | 72.33 | Highest 90 | Lowest 43 |
| Average Pulse Pressure | 17.91 | | |
| Average Mean Pressure | 78.10 | | |
| Average Pulse Rate standing | 111.67 | Highest 148 | Lowest 62 |
| Average Pulse Rate recumbent | 93.42 | Highest 140 | Lowest 64 |

| Group VI. | No. of Cases 30. | | Ages—35 to 40 yrs. |
|---|---|---|---|
| Average Systolic Pressure | 97.96 | Highest 135 | Lowest 75 |
| Average Diastolic Pressure | 74.96 | Highest 85 | Lowest 55 |
| Average Pulse Pressure | 23 | | |
| Average Mean Pressure | 82.63 | | |
| Average Pulse Rate standing | 107.03 | Highest 138 | Lowest 90 |
| Average Pulse Rate recumbent | 91.3 | Highest 119 | Lowest 70 |

| Group VII. | No. of Cases 29. | | Ages—40 to 45 yrs. |
|---|---|---|---|
| Average Systolic Pressure | 105.09 | Highest 165 | Lowest 75 |
| Average Diastolic Pressure | 80.63 | Highest 110 | Lowest 60 |
| Average Pulse Pressure | 24.46 | | |
| Average Mean Pressure | 88.78 | | |
| Average Pulse Pres. standing | 104.96 | Highest 130 | Lowest 82 |
| Average Pulse Pres. recumbent | 91.69 | Highest 112 | Lowest 62 |

| Group VIII. | No. of Cases 30. | | Ages—45 to 50 yrs. |
|---|---|---|---|
| Average Systolic Pressure | 106.80 | Highest 140 | Lowest 80 |
| Average Diastolic Pressure | 77.83 | Highest 115 | Lowest 62 |
| Average Pulse Pressure | 28.87 | | |
| Average Mean Pressure | 87.45 | | |
| Average Pulse Rate standing | 104.5 | Highest 126 | Lowest 68 |
| Average Pulse Rate recumbent | 93.73 | Highest 130 | Lowest 72 |

| Group IX. | No. of Cases 42. | | Ages—50 to 60 yrs. |
|---|---|---|---|
| Average Systolic Pressure | 105.29 | Highest 155 | Lowest 80 |
| Average Diastolic Pressure | 77.02 | Highest 115 | Lowest 55 |
| Average Pulse Pressure | 28.27 | | |
| Average Mean Pressure | 86.44 | | |
| Average Pulse Rate standing | 99.14 | Highest 121 | Lowest 80 |
| Average Pulse Rate recumbent | 89.52 | Highest 161 | Lowest 62 |

| Group X. | No. of Cases 26. | | Ages—60 yrs. and over. |
|---|---|---|---|
| Average Systolic Pressure | 114.34 | Highest 165 | Lowest 82 |
| Average Diastolic Pressure | 82.72 | Highest 105 | Lowest 60 |
| Average Pulse Pressure | 31.62 | | |
| Average Mean Pressure | 93.26 | | |
| Average Pulse Rate standing | 91.34 | Highest 112 | Lowest 65 |
| Average Pulse Rate recumbent | 80.57 | Highest 105 | Lowest 60 |

Under the first two groups the number of cases (three in each) is too small to justify an opinion. It will be noted that the pressure increases steadily until the highest point is reached in Group X in patients over sixty. This proportionate increase of pressure with advancing age accords well with the series of Thayer. The absolute lowering of pressure throughout the tuberculosis series is very marked. The comparison of the systolic pressure, found by Thayer in normal individuals at varying ages, with the systolic pressure met with in tuberculous patients of the same age, is of interest.

| | Normal Cases. | Tuberculosis Cases. |
|---|---|---|
| Ages | Systolic Pressure | Systolic Pressure |
| 10 to 20 yrs. | 128.7 | 100.33 |
| 20 to 30 yrs. | 136.9 | 101 |
| 30 to 40 yrs. | 140.8 | 94 |
| 40 to 50 yrs. | 142.2 | 105.5 |
| 50 to 60 yrs. | 154.8 | 105 |
| 60 to 70 yrs. | 180 | 114 |

The figures given for the T.B. cases are not absolutely accurate, but sufficiently so to show the contrast. While Thayer's figures are too high, as they were made with the narrow cuff, they are the best obtainable until the results of the work done at the University of Pennsylvania Gymnasium are published. This very constant lowering of the systolic pressure in the tuberculous cases throughout the various age periods is remarkable, particularly in the patients of forty years and over many of whom had been hard drinkers and whose arteries showed a high grade of arteriosclerosis. The number of cases (one hundred and twenty-seven over forty years of age) is so large that the question of a chance finding is eliminated. It remains to be proven whether this lowering of pressure is merely a secondary result of weakness or whether it is due to a direct and specific action of the tubercle bacillus or its

toxins upon the vaso-motor system. The very early occurrence of signs of vaso-motor relaxation in incipient tuberculosis is in favor of the latter possibility.

The behavior of the diastolic pressure in the different age periods is interesting. Unfortunately there are no observations upon normal individuals to serve as a comparison. So far as can be learned this is the first large series in which the diastolic pressure has been estimated. The variation is not great. The few cases showing a diastolic pressure below 70 were very close to death. The diastolic pressure in this series shows nearly the same proportionate increase with advancing age as that found with the systolic pressure. Hence there is also an increase in both the pulse pressure and mean pressure.

### BLOOD PRESSURE AND PULSE RATE

The relation between these two is not yet definitely settled. In the present series the pulse rate and blood pressure are given in connection with the age. It will be noted that while the pressure increases with age the pulse rate falls. This is apparently in accord with the theory advanced by Marey to the effect that increasing the blood pressure caused slowing of the pulse. It may be wise to point out here the variation in the pulse rate when standing and when recumbent. This difference is marked in the younger cases and is worthy of emphasis because it is of so much value in the prognosis and treatment. This postural pulse difference seems to be in inverse ratio to the pulse pressure. That is as the difference between the systolic and diastolic pressures increases the difference in pulse rate when standing and lying diminishes.

### BLOOD PRESSURE IN TUBERCULOSIS AND PREVIOUS POISONS AND INFECTIONS

Alcohol.—Male cases giving history of excessive use of alcohol, 74; male cases giving history of moderate use of alcohol, 74; female cases giving history of excessive use of alcohol, 9; female cases giving history of moderate use of alcohol, 8. Total, 165.

More than two-thirds of the total number of cases showed more

or less habitual use of alcohol. The number of cases in each age group is given together with the average pressure of the alcoholics. It will be noted that in nearly all instances the systolic pressure of drinkers is relatively high. The diastolic pressure is on the upper limits of the group level, but is not so high as one would expect in habitual drinkers.

Infections.—*Gonorrhœa.*—There were 64 cases in males and 8 in females. The latter figure may be open to doubt. These cases are on the upper bounds of pressure of their respective groups. This coincidence is merely pointed out. It is practically impossible to separate the venereal cases from the alcoholics.

*Syphilis.*—Male, 34; female cases, 1. Attention may be called again to the difficulty in securing a history of venereal disease in women. The pressure of the syphilitics in comparison with that of the age group is given. The systolic pressure is relatively high in groups III, IV, V and VIII; relatively low in groups VI, VII, IX and X. The diastolic pressure acts in the same manner except in group X, where it is slightly higher proportionately.

*Typhoid Fever.*—Male cases, 26; female cases, 10. Total, 36.

This is about 11 per cent. of the series and is rather less than the Phipps Institute report of 13 per cent. in the first year and 18 per cent. in the second year. As Thayer has reported an increase of systolic pressure in those who have had typhoid fever, the comparison here is of interest. In the present series this increase of sytolic pressure is met with in all groups except groups III and VIII. The diastolic pressure is proportionately high in all except III. This is so even in group VIII where the systolic pressure is low.

*Pneumonia and Blood Pressure.*—Cases: male, 27; female, 14. Total, 41. The systolic pressure is high in males in groups V, VI, X; 17 cases. The diastolic pressure is normal in males in groups V, VI, X; 17 cases. The systolic pressure is low in males in groups IV, VII, VIII, IX; 10 cases. The diastolic pressure is low in males in groups IV, VII, VIII, IX; 10 cases. The systolic pressure is high in females in groups 5, 6, 7, 8, 9; 8 cases. The diastolic pressure is high in females in groups 7, 8, 10; 5 cases. The systolic pressure low in females in groups 3, 4, 9, 10; 6 cases. The diastolic pressure low in females in groups 4, 5, 6, 9; 9 cases.

Romberg and Passler found that death in pneumonia was due to the action of the toxin on the vaso-motor system, and it would be of interest to know whether any permanent effect was made on the blood pressure. From this series the males show normal or increased pressure both systolic and diastolic in 17 cases. Both pressures are lower in 10 cases. In the females 8 cases show high systolic and 6 cases low systolic. Five cases show high diastolic and 9 cases low diastolic.

*Diphtheria and Blood Pressure.*—(15 cases.) These are too few to be of interest.

### BLOOD PRESSURE AND DEGREE OF INVOLVEMENT

An attempt was made to bring the degree of involvement of lung tissue, after the plan of Turban, in accord with the blood pressure. This was found to be impossible. There is no apparent relation. With regard to the outcome of the disease and its relation to the blood pressure 72 cases were analyzed. It was impossible to cover all the cases as a portion of the histories are at the binders.

Improved cases, 31; average systolic pressure, 112; average diastolic pressure, 79.38; in hospital doing fairly well, 9 cases; average systolic pressure, 115.22; average diastolic pressure, 80.

Unimproved, 8 cases; average systolic pressure, 103.125; diastolic pressure, 79.38; died, 24 cases; average systolic pressure, 96.25; diastolic, 68.38. These cases show very plainly the diminution of both pressures in advancing cases.

### BLOOD PRESSURE AND NEPHRITIS

With a view to determining the effect of the very frequent nephritis of the tuberculous upon the blood pressure 21 cases were specially studied. The eyes of 9 of these cases were examined by Dr. de Schweinitz to see if the changes were of the kind ordinarily found in nephritis. At the same time note was made of the heart sounds, pulse rate, and other points that might show the increased pressure so frequently associated with kidney disease.

There were 21 cases in which the urine showed albumin and casts. Of these 10 were males and 11 females. Of the male

cases 1, aged sixty-five, had hard arteries and a distinct diastolic murmur over the aortic area. The systolic pressure was 165; diastolic pressure 95. Another, aged seventy, with a distinct arteriosclerosis, gave a systolic pressure of 145, diastolic pressure of 120. The remaining 8 cases showed an average systolic pressure of 96.87 and a diastolic pressure of 74.75. As evidence of disturbed circulation there was noted a systolic mitral murmur in 1; accentuation of the pulmonic second sound in 1; accentuation of the aortic second sound in 1; the average pulse rate standing 100.67; highest, 128; lowest, 76; average pulse rate recumbent, 89.3.

The 11 female cases with urinary signs of nephritis showed an average systolic pressure of 92; an average diastolic pressure of 77. As evidence of disturbed circulation 1 showed a mitral systolic murmur when recumbent; 1 a reduplicated first sound; 7 an apparent accentuation of the pulmonic second sound; the average pulse rate in the erect position in 7 cases was 107 3-7; highest, 136; lowest, 88. Average pulse rate recumbent was 96; highest, 122; lowest, 80.

The eye grounds in 9 of these nephritic cases were examined by Dr. de Schweinitz. The results are given in detail.

C. N., aged 65, male. Marked evidences of kidney disturbance for two years. Systolic pressure, 90; diastolic pressure, 75; pulse rate erect, 92; recumbent, 72. Eye grounds: bilateral vitreous opacities; fundus details hazy; dilated retinal veins; beginning pressure signs.

J. Mc. G., aged 33, male. Systolic pressure, 90; diastolic pressure, 72; pulse rate erect, 102; recumbent, 84. Eye examination. O.D. Corneal opacity; disc hazy; veins enormously swollen; light streak more distinct than normal. Some tortuosity of transverse vessels, no positive indentation. O. S. shows same changes.

N. J., aged 38, female. Systolic pressure, 95; diastolic pressure, 80. Pulse rate erect, 100; recumbent, 94. Partial cataract of both eyes obscures fundus. Some dilatation of the veins.

A. H., aged 44, female. Systolic pressure, 90; diastolic pressure, 72. Pulse rate erect, 88; recumbent, 80. Accentuated pulmonic second sound. O. D. shows myopia of 4 d. Disseminated choroiditis. No vascular abnormalities.

L. C., aged 30, female. Systolic pressure, 90; diastolic pressure, 70. Pulse rate erect, 108; recumbent, 84. Eye grounds show small disc; dilated tortuous veins; increased distinctness of the light streak; typical indentation of the veins by the arteries.

M. S., aged 31, female. Systolic pressure, 125; diastolic pressure, 95. Pulse rate erect, 136; recumbent, 122. Eye grounds: O. D. no arteriosclerotic change. O. S. similar. Veins were dilated but there were no further vascular changes.

J. C., aged 65, male. Systolic pressure, 165; diastolic pressure, 95. Pulse rate erect, 112; recumbent, 90. There was a distinct diastolic murmur over the aortic area and the arteries were hard. Eye examination. O. D. disc hazy and markedly swollen; veins uneven; distinct early pressure signs. A patch of choroiditis near the macula possibly tuberculous. O. S. similar; veins even more tortuous and swollen; very slight pressure signs; no change in disc.

H. B., aged 70, male. Systolic pressure, 145; diastolic pressure, 120. Pulse rate erect, 80; recumbent, 70; arteries hardened. Eye examination: Media clear; disc rather pale; veins larger than normal; light streak on arteries sharply marked; just beginning indentation; macula studded with discrete and confluent yellowish-white areas apparently colloid.

H. McG., aged 55, male. Systolic pressure, 95; diastolic pressure, 70. Pulse rate erect, 100; recumbent, 86. Eye examination: O. D. bilateral corneal opacities. O. S. slight choroiditis; vessels suggest only slight pressure signs.

The chief point of interest in these cases of nephritis is the very low pressure averages. Again the question arises as to whether the weakness of the patient is responsible or whether the specific action of the tubercle bacillus is the causal factor. While only the most marked cases of urinary disturbance are mentioned here, they do not by any means represent the proportion with kidney involvement. The studies of Walsh, made at the Henry Phipps Institute, go to show that the majority of patients with advanced tuberculosis have distinct kidney involvement. This involvement is not often associated with enlargement of the heart nor, as we would expect, with increased blood pressure. The two cases showing heightened pressure presented complications—aortic regurgita-

tion in 1, and arteriosclerosis in the other—which very readily account for this increase. It seems to be fairly certain that the nephritis of tuberculosis does not effect the blood pressure.

### BLOOD PRESSURE AND HÆMORRHAGE

Hensen first stated that the blood pressure was increased in the hæmorrhage of pulmonary tuberculosis, but he only had 1 case and used this as an argument against the use of the sphygmomanometer. Various observers have noted the frequency of an apparently accentuated second sound in phthisis patients with hæmorrhage and from this have assumed a high blood pressure. Recently Lawrason Brown has advocated the treatment of hæmorrhage by using sodium nitrite in sufficient amount to keep the blood pressure (presumably systolic) between 100 and 120 M.M.

The cases of hæmorrhage upon which I have notes are from the Phipps Institute and are only five in number. In only one of these did the systolic pressure reach 120. In this case the systolic pressure, which was taken repeatedly at other times varied between 112 and 115. The occurrence of a slight rise in pressure after the spitting of blood is readily explainable upon the ground of excitement. Case No. 3873, Phipps Institute, had been spitting blood daily with occasional true hæmorrhage for two months. He showed a systolic pressure which varied between 100 and 108. Phipps Institute case, No. 4142, September 23, 1906, systolic pressure 102. He had a hæmorrhage on September 22, 1906, and the sputum was still pink. September 24, 1906, systolic pressure 95, no blood. October 15, 1906, systolic pressure 90. Hæmorrhages on October 13, 1907, and October 14, 1907.

Of course the blood pressure estimations show only the condition of the systemic pressure and it is possible that the pulmonary pressure may be increased. This is borne out by the frequent finding of an apparently accentuated second sound over the base of the heart. Autopsy records, however, fail to show any constant enlargement of the right heart, and from personal observations, increase in the pulmonic pressure seems to me doubtful. The slight increase in systolic pressure after hæmorrhage seems likely to be due to excitement, increased cough and perhaps a stimulation of the vasomotor centre from hæmorrhage with consequent vaso-constriction.

## EFFECT OF DRUGS AND INFECTIONS ON PRESSURE.

| AVERAGE GROUP PRESS. | | | ALCOHOL | | GONORRHŒA | | SYPHILIS | | TYPHOID | | PNEUMONIA | | DIPHTHERIA | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Group. | Syst. | Diast. | Syst. | Diast. | Syst. | Diast. | Syst. | Diast. | Syst. | Diast. | Syst. | Diast. | Syst. | Diast. |
| 3. 20-25 years.... | $99\frac{5}{15}$ | $73\frac{3}{15}$ | Excess. Cases 2<br>$97\frac{1}{2}$ | 65 | No. Cases 1<br>107 | 80 | No. Cases 1 f.<br>113 | 85 | No. Cases 1<br>84 | 45 | No. cases 1 f.<br>95 | 73 | | |
| 4. 25-30 years.... | $103\frac{7}{16}$ | $75\frac{14}{16}$ | Excess. Cases 5<br>102<br>Moderate Cases 3<br>$106\frac{2}{3}$ | $73\frac{3}{5}$<br>$75\frac{1}{3}$ | Male Cases 2<br>105<br>Female Cases 1<br>118 | 79<br>78 | Male Cases 2<br>$107\frac{1}{2}$ | $82\frac{1}{2}$ | Male Cases 1<br>115<br>Female Cases 2<br>115 | 90<br>85 | Male Cases 3<br>100<br>Female Cases 1<br>75 | $74\frac{1}{3}$<br>58 | | |
| 5. 30-35 years.... | $90\frac{5}{26}$ | $72\frac{2}{27}$ | Excess. Cases 8 m.<br>98<br>Moderate Cases 6<br>$102\frac{1}{2}$ | $73\frac{7}{8}$<br>$77\frac{2}{5}$ | Male Cases 4<br>100 | 76 | Male Cases 5<br>102 | $76\frac{2}{5}$ | Male Cases 1<br>95<br>Female Cases 3<br>$97\frac{2}{3}$ | 72<br>$72\frac{3}{3}$ | Male Cases 5<br>$97\frac{2}{5}$<br>Female Cases 2<br>$96\frac{1}{2}$ | 75<br>68 | Male Cases 1<br>$97\frac{2}{5}$<br>Female Cases 2<br>99 | 75<br>$76\frac{1}{2}$ |
| | | | Excess. Cases f. 4<br>92<br>Moderate Cases f. 2<br>$111\frac{1}{2}$ | $60\frac{1}{4}$<br>$77\frac{1}{2}$ | | | | | | | | | | |
| 6. 35-4 years.... | $97\frac{23}{30}$ | $74\frac{23}{30}$ | Excess. Cases 11 m.<br>100<br>Moderate Cases 8<br>$102\frac{3}{4}$<br>Excess. Cases f. 1<br>90<br>Moderate Cases f. 4<br>103 | $74\frac{11}{13}$<br>$76\frac{5}{8}$<br>70<br>75 | Male Cases 14<br>$98\frac{1}{14}$ | $72\frac{5}{7}$ | Male Cases 3<br>95 | $71\frac{2}{3}$ | Male Cases 4<br>105<br>Female Cases 3<br>$112\frac{1}{3}$ | 75<br>80 | Male Cases 5<br>$110\frac{2}{5}$<br>Female Cases 3<br>94 | 83<br>$73\frac{1}{3}$ | Male Cases 2<br>$111\frac{1}{3}$<br>Female Cases 3<br>$87\frac{1}{3}$ | 82<br>69 |
| 7. 40-45 years.... | $105\frac{3}{29}$ | $80\frac{21}{29}$ | Excess. Cases m. 8<br>$106\frac{7}{8}$<br>Moderate Cases 6<br>103 | $81\frac{7}{9}$<br>$77\frac{15}{16}$ | Male Cases 11<br>$106\frac{2}{11}$ | $77\frac{1}{11}$ | Male Cases 4<br>$99\frac{1}{2}$ | $76\frac{1}{4}$ | Male Cases 5<br>$112\frac{2}{6}$<br>Female Cases 1<br>115 | $82\frac{2}{6}$<br>85 | Male Cases 1<br>$104\frac{5}{7}$<br>Female Cases 1<br>115 | $78\frac{2}{7}$<br>85 | Male Cases 2<br>$122\frac{1}{2}$ | 90 |

EFFECT OF DRUGS AND INFECTIONS ON PRESSURE.—*Continued.*

| Group. | AVERAGE GROUP PRESS. Syst. | Diast. | ALCOHOL Syst. | Diast. | GONORRHŒA Syst. | Diast. | SYPHILIS Syst. | Diast. | TYPHOID Syst. | Diast. | PNEUMONIA Syst. | Diast. | DIPHTHERIA Syst. | Diast. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 8. 45-50 years.... | $106\frac{24}{30}$ | $77\frac{25}{30}$ | Excess. Cases m. 14<br>$105\frac{1}{14}$ | $78\frac{13}{14}$<br>Moderate Cases 11<br>$111\frac{7}{11}$ | $80\frac{0}{11}$<br>Excess. Cases f. 1<br>95 | 70<br>Moderate Cases f.<br>100 | 80 | Male Cases 13<br>$102\frac{10}{13}$ | $76\frac{0}{13}$ | Male Cases 4<br>$112\frac{1}{4}$ | $83\frac{1}{4}$ | Male Cases 3<br>$102\frac{2}{3}$ | $78\frac{1}{3}$ | Male Cases 2<br>100 | $77\frac{1}{2}$<br>Female Cases 2<br>120 | $97\frac{1}{2}$ | Male Cases 1<br>95 | 75 |
| 9. 50-60 years.... | $105\frac{12}{42}$ | $77\frac{1}{42}$ | Excess Cases m. 18<br>$110\frac{2}{3}$ | $83\frac{8}{9}$<br>Moderate Cases 18<br>$100\frac{8}{9}$ | $74\frac{13}{18}$<br>Excess. Cases f. 3.<br>111 | $81\frac{2}{3}$ | Male Cases 13<br>$104\frac{2}{13}$ | $76\frac{1}{13}$ | Male Cases 13<br>$104\frac{2}{13}$ | $76\frac{1}{13}$ | Male Cases 6<br>110<br>Female Cases 1<br>118 | $77\frac{3}{3}$<br>90 | Male Cases 14<br>$102\frac{0}{14}$<br>Female Cases 2<br>$101\frac{1}{2}$ | $77\frac{1}{2}$<br>$72\frac{1}{2}$ | Male Cases 1<br>100<br>Female Cases 1<br>118 | 85<br>90 |
| 10. Over 60..... | $114\frac{14}{20}$ | $82\frac{24}{20}$ | Excess. Cases m. 10<br>$116\frac{4}{8}$ | $83\frac{0}{16}$<br>Moderate Cases 12<br>$110\frac{1}{3}$ | $80\frac{5}{6}$<br>Moderate Cases f. 1<br>110 | 87 | Male Cases 8<br>$103\frac{5}{8}$ | $77\frac{3}{8}$ | Male Cases 3<br>$111\frac{2}{3}$ | $83\frac{2}{3}$ | Male Cases 5<br>$114\frac{3}{8}$ | $83\frac{1}{8}$ | Male Cases 7<br>$116\frac{3}{7}$<br>Female Cases 2<br>115 | $87\frac{5}{7}$<br>$82\frac{1}{2}$ | Male Cases 1<br>105<br>Female Cases 1<br>110 | 80<br>87 | | |

Total Male Excess. Cases ..... 74
Total Male Moderate Cases ..... 74
148

Total Female Excess Cases..... 9
Total Female Moderate Cases ..... 8
17

The deductions which the present study seem to justify may be summarized as follows:

1. The blood pressure in tuberculosis is generally low. This applies to both systolic and diastolic pressures.

2. It is slightly lower in females than in males. This is true of all pressures.

3. The blood pressure increases steadily from childhood to old age. This increase is greater in the systolic pressure than in the diastolic pressure; hence as age advances, the pulse pressure increases.

4. The blood pressure in tuberculosis bears an inverse ratio to the pulse rate. The pulse rate is higher in childhood and lower in old age. The difference between the pulse rate when standing and lying tends to diminish with age.

5. Time of day, presence of fever, degree of involvement, have no influence on the blood pressure of tuberculosis.

6. The blood pressure is higher in improving cases and lower in progressing and unfavorable cases.

7. Alcoholics with tuberculosis show a somewhat higher systolic pressure than the total for the series, the difference is about equal to that found between males and females.

8. Gonorrhœa and syphilis show no positive effect on tuberculosis; they cannot be separated from the alcoholics.

9. Typhoid fever seemingly causes a higher pressure in the victims. Both systolic and diastolic pressures are increased. The diastolic rather more than the systolic.

10. The nephritis of tuberculosis apparently does not increase the blood pressure.

11. Hæmorrhage is apparently not accompanied by increased pressure.

# TWO CASES OF PRIMARY CARCINOMA OF THE LIVER: ONE WITH FIBRINOUS PNEUMONIA; ONE DIAGNOSTICATED BY PARACENTESIS ABDOMINIS

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In this paper we shall deviate a little from the ordinary clinical course and deal more with the absolute and indisputable facts in medicine. As the basis of this article we have two rare and interesting cases.

The first case, a man about fifty years of age, had had the symptoms about to be described over a period of four years. When first seen in 1898, about a year before he died and three years after the development of his first symptoms, he complained of some pain and a feeling of enlargement in the region of the liver. There were also symptoms of a general disturbance of the hepatic function. There was a slight jaundice and a sallow appearance of the skin. He said he could feel the enlargement in the hepatic region and that it had been apparent to him for the past two years, and so far as he could judge he was getting larger in that region. On account of the prolonged duration of the symptoms, it did not seem probable that the enlargement could be due to a carcinomatous growth—the general belief at that time being that visceral carcinomatous growths were apt to be of very short duration. At the same time, he had a pronounced cachexia.

On physical examination it was found that the liver was greatly enlarged, the organ being at least twice its normal size. On the anterior surface of the left lobe two very prominent points were observed. They were easily seen and felt through the somewhat thinned abdominal wall. Upon palpation the nodules were found to be soft and fluctuating. A trocar was introduced into one of

them and some fluid withdrawn. In the fluid were found hepatic cells stained with bile pigment and numerous cells resembling those from a carcinomatous growth. Prof. Henry T. Brooks examined the cells and declared that they were cancerous in character, and that the patient must have a carcinoma of the liver. The writer therefore had to disregard his previous opinion and admit that there was a carcinoma of the liver, though even then a primary carcinoma of the liver was not suspected though we were sure that the liver was invaded by a new growth, on account of the bile-stained hepatic cells. So far as can be ascertained, this is the first case in which the diagnosis of cancer of the liver was made by paracentesis abdominalis directly into the tumor.

In two or three instances before this the diagnosis of carcinoma had been made by paracentitis and examination of the fluid withdrawn. In all, about eight cases have been recorded in which the diagnosis was made by this method of examination.

Three or four months after the puncture the man died. The liver was secured, and the specimen was found to be an exceptionally fine and typical example of a primary carcinoma of the liver. Figure 1 is a perfect illustration of its appearance under the microscope. The neoplasm had involved nearly two-thirds of the liver. It was the first case of primary carcinoma of the liver that the writer had ever seen.

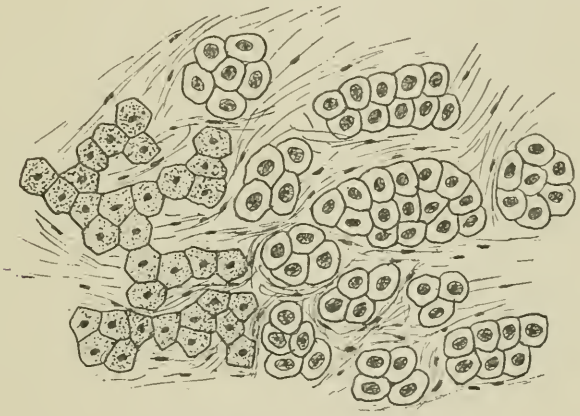
The liver was presented at the Stated Meeting of the New York Pathological Society, held December 14, 1898, and a report of the case published in the transactions of the Society for 1897 and 1898.[1] The specimen was also shown at a meeting of the New York Medico-Surgical Society at about the same time.

The second case was that of a man fifty-six years of age. He had an enlargement at the root of the neck on the right side, and when first seen by the author it was apparent that he had had an eye abstracted a few months before. On percussion he had all over the right side of the chest, up to the third rib, absolute flatness, both anteriorly and posteriorly. He was suffering a good deal from dyspnœa and gave the history of losing flesh very rapidly during the past five or six weeks. He had been to one of the throat clinics, where a diagnosis of a partial paresis of the right vocal cord was recorded. At the time when first seen it was evident that the patient

had fluid in the pleural cavity as the causative factor in producing the flatness. It was also thought that the dullness might be the result of a neoplasm within the chest cavity, either a sarcoma or a carcinoma originating in the mediastinal space or in the lung; or that it might be the result of a chronic pleurisy. It seemed certain that part of the dullness, at least, was due to fluid.

In September the patient went to the office of Dr. E. L. Oatman, of Brooklyn, an able oculist. At that time he gave the history of progressive loss of vision in the right eye, which was followed by a marked hardening of the eyeball and considerable pain. Dr. Oatman made the diagnosis of an intra-ocular tumor of the eye, and removed the eyeball.

FIG. 1.



Primary carcinoma of the liver.

A careful microscopic examination of the eyeball revealed a carcinomatous growth springing from the coroid. The neoplasm had invaded and destroyed the interior of the globe, although externally the eye presented a normal appearance. Dr. Oatman, commenting on the case, made the following statement: "This is a pathological curiosity, and but few oculists have ever seen such a condition." (See Fig. 2.) It was a peculiar growth: it was an interpapillary adenocarcinoma, a condition that we see constantly in ovarian cysts, tumors which have undergone carcinomatous change within the cyst. Figs. 3 and 4 show extension of the carcinoma into the retina and optic nerve.

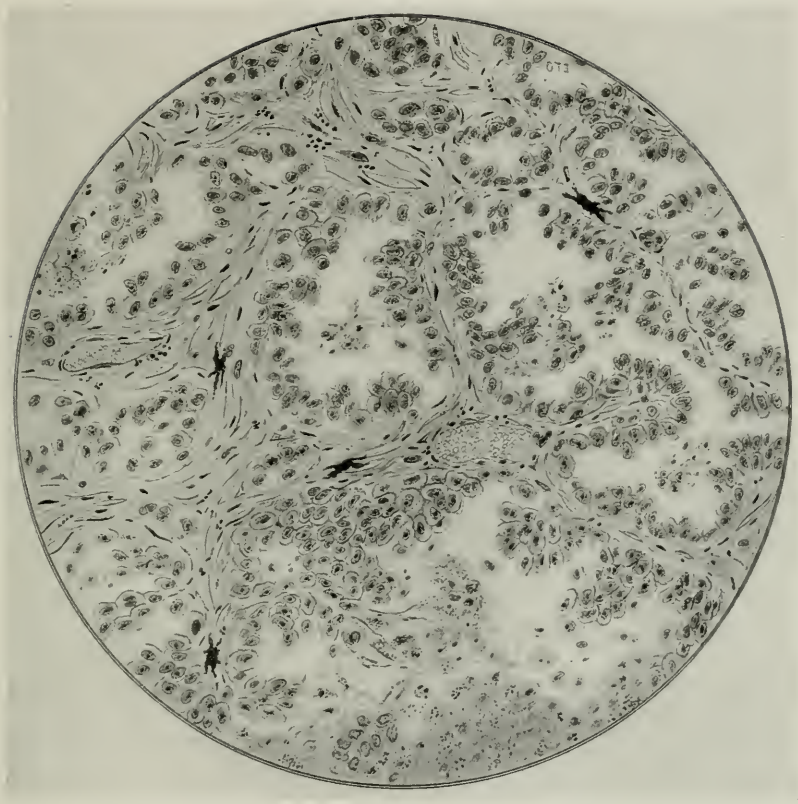
Finding these symptoms and physical signs in the chest in conjunction with the known condition in the eye, the physician, who originally had charge of the case, supposed that the growth had possibly taken its origin in the lung. So far as known, a primary carcinoma of the eyeball had never been recorded. In fact, there is no epithelial structure in the eyeball proper from which such a neoplasm could spring.

There must always be an epithelial tissue to cause the development of this type of growth. In all his experience the writer has never seen but one case of a carcinomatous nature in connection with the eye, and that was a "Melanotic epithelioma" of the cornea which occurred in the practice of the late Dr. Henry D. Noyes.[2] In that instance the neoplasm took its origin in the conjunctiva and not in the cornea, although it infiltrated the latter.

When examining this carcinomatous neoplasm of the eyeball under the microscope, Prof. Henry T. Brooks and Dr. Oatman, whose case it was, came to the conclusion, from the character of the epithelial cells composing the growth, that it was secondary in its nature, and that it had taken its origin from a primary growth along the line of one of the mucous membranes,—from either the bronchial or pulmonary mucous membrane, or from that of the alimentary tract. The view uppermost in their minds, however, was that it came from the abdominal rather than from the pulmonary region, and from the peculiar character of the epithelial cells they were inclined to believe that it took its origin in the liver. Some of the sections which the writer had the pleasure of examining looked almost as if a section of the liver was under the microscope, yet it was clear that it was not composed of hepatic cells, but those of a cancerous nature that were in the field. Knowing the extreme rarity of primary cancer of the liver, they were not in a position to say positively that this secondary growth had taken its origin from a primary neoplasm in the liver.

The patient was sent into the Post Graduate Hospital on the 30th of November, 1901. The following is a brief history of the case while in the ward: The patient is pale, emaciated, and has a cachectic appearance. There is marked dyspnœa, and difficulty in swallowing solid food. Respiration is rapid and superficial, most marked on the right side. Inspection shows a pronounced enlarge-

FIG. 2.



Interpapillary adenocarcinoma. × 500. From original drawing by Dr. E. L. Oatman.

FIG. 3.

Extension of carcinomatous growth to ora serata. × 100.

FIG. 4.

Carcinomatous invasion of optic nerve and retina. × 100.

ment at the root of the neck on the right side. This tumefaction appears to be due to enlargement of the deep cervical glands. The apex beat of the heart is in the normal position. In the supra- and infra-clavicular regions, on the right side of the chest, there is decreased vocal fremitus and increased respiratory murmur. In the pectoral and axillary regions there is absence of fremitus; exaggerated breathing above the level of the third rib,—here the percussion note is abnormally resonant. Below this region percussion reveals marked dullness, or, more strictly speaking, flatness all over the chest, both anteriorly and posteriorly. The flat character of the note suggests the presence of fluid in the pleural cavity. Auscultation reveals absence of vocal fremitus and all respiratory sounds over the flat area. Posteriorly, in the supra-spinous region, the respiratory murmur is slightly increased. There is also dullness on percussion. Over the infra-spinous region there are heard distinct respiratory sounds. There is exaggerated breathing over the whole left side of the thorax anteriorly; the vocal fremitus is exaggerated, and the percussion note is abnormally resonant. Posteriorly, a few subcrepitant rales are distinctly heard. The superior margin of hepatic dullness could not be determined. The inferior margin is eight (8) centimetres below the free borders of the ribs. Spleen and kidneys negative, so far as physical examination is concerned.

On December 1st, the right pleural cavity was aspirated and 22 ounces of yellow, faintly blood-tinged fluid withdrawn. Microscopic examination of the aspirated fluid showed no tubercle bacilli or cells indicative of a neoplasm. Sputum blood-stained; tubercle bacilli not found. Microscopic examination of the fresh unstained sputum showed numerous red blood corpuscles, a moderate number of pus cells, occasional flakes of squamous epithelia, and stray cells of an atypical epithelioid character resembling glandular epithelial elements. The latter were not sufficiently numerous to support the suspicion of a neoplasm in the respiratory apparatus.

After the withdrawal of the fluid the chest was again carefully examined, and no change found in the physical signs. The continuance of the physical signs tended to support the theory of a new growth in the chest cavity; at the same time, the microscopic evidence was against such an interpretation of the signs.

Urine examination showed no albumin and no sugar; specific gravity, 1,008; numerous uric acid crystals and deposits of urates.

December 2. Coughs a great deal; complains of pain in the right side of the chest. Morning temperature, 98°; pulse, 100; respirations, 20. Evening temperature, 102°; respirations, 31.

December 3. Urine shows no albumin; occasional small hyaline and fine grandular casts; no deposit of uric acid or urates; specific gravity, 1,025.

Up to December 7th no notable feature presented. At 6 P.M. patient complained of great pain through the right side of the chest; temperature 101.8°; pulse 108; respirations 32.

December 8th. At 7 A.M. vomited food; respirations 38 and labored. In right supra- and infra-clavicular regions to the third rib there are noted increased fremitus, dullness, bronchial breathing, increased voice sounds, and crepitant and subcrepitant rales. Posteriorly the supra-spinous and inter-scapular regions present the same physical signs. 10 P.M., temperature 103.3°; pulse 120, weak; respirations 36; coughs a great deal.

December 9, A.M. Slept fairly well, though slightly delirious. Temperature 102°; pulse 116; respirations 36. Urine very dark red, non-albuminous. Coughs much. Great pain through the abdomen. Anorexia. Stools dark and loose. Widal test, negative. Careful microscopic examination of the blood failed to reveal malarial organisms.

December 10. Drowsy all day.

December 11. Respirations difficult, with transitory attacks of dyspnœa and cyanosis, which were relieved by hypodermic injections of strychnia and atropin; temperature 102.8°; pulse 132, weak; respirations, 32.

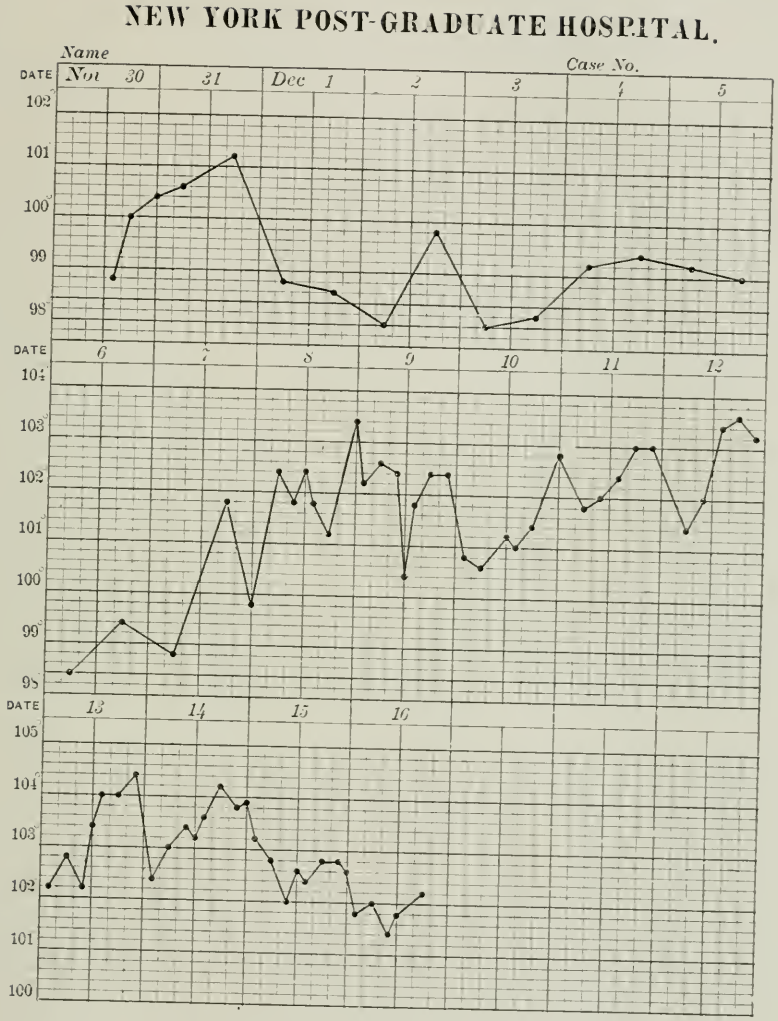
December 12. Tongue and mouth very dry; slight delirium; temperature 103.6°; pulse 108; respirations, 36.

December 13. Delirious at intervals all night; difficult to raise mucus from the throat. Pulse 104, very weak; respirations, 40, very difficult; temperature 102.8°.

December 14. Delirious all night; great dyspnœa; temperature, 104.2°; respirations, 40; pulse, 120.

December 15. Temperature 103.2°; pulse, 108, very weak; respirations, 40; dyspnœa; delirious.

FIG. 5.


NEW YORK POST-GRADUATE HOSPITAL.
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December 16. Labored breathing; cyanosis; unable to raise mucus from throat; profuse cold perspiration; violent paroxysms of coughing, which are partially relieved by hypodermic injections of nitro-glycerine and atropin, and by oxygen inhalation. Temperature 103.2°; pulse, 138, very weak and compressible; respirations, 48. At 7.30 P.M. patient died. (See temperature sheet, Fig. 5.)

We now come to the study of the specimens removed at the necropsy. The heart showed nothing abnormal save the ordinary atrophic condition of the muscle fibres commonly found in connection with all wasting diseases. When we come to the lung, or rather to the contents of the right thoracic cavity, we find that the man had suffered—probably in years gone by—from an old pleurisy which had given rise to a good deal of thickening of the pleura over the lung and on the costal side. The two surfaces of the pleura were also adherent at various points, so that it gave rise, as it were, to little attachments of the pleura between the lung and the chest wall in this manner confining the fluid in separate chambers. There could readily be seen a certain amount of carnification at the inferior portion of the right lung. This very decided thickening of the pleura, with the carnification of the lung and the serous effusion into these chambers, easily explained the reason for the decided dullness during life, even after the withdrawal of the fluid, and yet there was no macroscopic evidence of a new growth within the chest cavity at the necropsy.

On the other hand, it is easy to see from the history and the conditions found at the necropsy how very difficult it is to be absolutely sure as to just what exists during life under the chest wall, and still more so under the abdominal parietes. There is no question about dullness that we can make out; and there is no question about absence of breathing and there is no question about the presence of exaggerated breathing above the area of dullness; but there are times when it is extremely difficult, if not absolutely impossible, to say exactly what the condition is that causes the indisputable signs. It is particularly so when we have conditions in connection with the history which lead us, as we had a right to be led in this case, to suspect the possibility of a carcinomatous growth within the chest cavity as the primary neoplasm which was probably acting as the cause of the secondary growth

known to exist in the eye. The necropsy in this case, as in almost every instance, furnishes a clear explanation for the physical signs that were present—the dullness, the flatness, the absence of breathing, together with the continuance of the dullness after the withdrawal of the fluid from the chest cavity. The writer is confident that we can always be certain of fluid under the chest wall if we recognize the difference between flatness and dullness. To some it may appear absurd to make this sharp distinction between flatness and dullness, but there is a decided difference between the percussion note elicited over a fluid and a solid which is albuminous in character.

Whenever there is a fluid under the chest wall, there is a peculiar flatness to the percussion note, and it was this peculiar flatness of the note which led the writer to say that he was sure if an aspirating needle was inserted in the man's chest fluid would be withdrawn. When the chest was aspirated, this opinion was sustained. The lung was materially carnefied because of the pleurisy with effusion which had probably existed for a considerable period of time—a condition which had nothing to do with the carcinomatous development, since it was a coincident lesion and one that had developed before the patient began to suffer from the carcinoma. Otherwise there would not be this extensive fibrous thickening of the pleura.

At the necropsy, we found that the direct cause of his death was the small area of fibrinous pneumonia which had attacked a small part of the remaining portion of the uncompressed lung. In other words, as the result of his lowered nutritive vitality, and as a result of the localization of this lowered nutritive vitality in his previously damaged lung, a slight congestion had developed, and in consequence of these three conditions a soil was produced in the pulmonary tissue that was suitable for the development of a typical infectious pneumonia.

Further and careful investigation of all the organs in the chest cavity and mediastinal spaces showed no marked macroscopic evidence of a primary carcinomatous neoplasm. A few small deposits, microscopic in character, were found in the bronchial mucous membrane on the right side. These microscopic growths could not, however, be regarded as primary in origin but as secondary in nature.

Fig. 6.

Liver with primary and secondary carcinomatous deposits.

A careful scrutiny of the whole line of the alimentary tract failed to reveal the presence of a primary carcinomatous neoplasm at any point along the line of this canal. In the liver, however, there were several well-defined carcinomatous masses. (See Fig. 6.)

The peculiarity of the carcinomatous growths in the two cases is that they assumed the general outlines of the liver acini. That the carcinomatous growth replaced the acinus structure of the liver was easily demonstrated in both cases. This was especially clear in the first case. Had we been fortunate enough in the second case as we were in the first to have located the growths in the liver during life, we could have introduced a trocar, and judging from the results obtained in the first case, would probably have withdrawn some of the carcinomatous cells and thus located and diagnosticated the primary growth in the liver. In the first case it was done, and a correct diagnosis made so far as the nature of the neoplasm was concerned, but we were not able to say that it was primary in the liver. In future cases it may be possible to locate the primary growth by the peculiar type of the cells found in the fluid withdrawn from the tumor. There is no question after studying the necropsy findings that in both cases the primary growth was in the liver. All the other nodules found in the various parts of the body in the second case took their origin from the primary neoplasm in the liver. Figs. 2, 3 and 4 show the secondary growth in the eye.

The kidneys in the second case were the seat of a few infiltrations—nine in the right and one in the left gland—carcinomatous in character. The kidneys were a little larger than normal, and presented the appearances commonly found in these organs in connection with wasting diseases. Their capsules were rather adherent, which showed that there was a slight amount of interstitial involvement. The epithelial cells were a little swollen and unduly granular. The change in the epithelial cells was that of a mild parenchymatous degeneration, which together with the interstitial involvement makes the lesion diffuse in character.

The spleen contained one small carcinomatous nodule; the same was true of the brain and the meninges.

Both cases are of great interest on account of their rarity and the completeness with which the new growth displaced the liver acini. The second is of especial interest on account of the peculiar

and unique course which the disease pursued, and the rare point of development in the eye. At one time we were led to believe that the transmission of carcinomatous neoplasms from place to place was by the lymphatic channels only. This case absolutely disproves such a theory, for there is no line of lymphatics running from the liver to the eye, and hence that method of transmission has to be excluded. The probabilities are, therefore, that the only way in which this new growth in the liver could be transmitted to the ocular region was along the line of the blood channels. The cells constituting the carcinomatous growth breaking through from the hepatic acinus structure of the liver into the hepatic veins, passing in the blood stream through the inferior vena cava, through the heart, and finally passing through the lungs, and on to the cephalic vessels, for some reason or other found lodgment in the posterior portion of the eyeball. At this point the carcinomatous cells met some capillary blood vessels which were too small to allow their transit, and in which the soil was suitable for the growth of the carcinomatous neoplasm. This is the only way in which we can rationally explain the secondary deposits in the eye.

Eighteen or twenty years ago the common teaching was to the effect that there was no such thing as a primary carcinoma of the liver; that every carcinomatous growth found in this organ was secondary to a primary neoplasm in some other portion of the body. These two cases, however, taken alone certainly establish beyond question or doubt that such teaching was erroneous. In addition to this Hugo Eggel in 1901 collected and recorded 163 cases of primary cancer of the liver.[3] Since that time there have been added 47 more cases, making a total up to date of 210 cases. Nevertheless it is true, that primary carcinomata of the liver are exceedingly rare. Owing to their infrequency and the great frequency of secondary growths of this nature in the liver, it is not to be wondered at that the general impression was so long retained that primary carcinoma did not occur. During a period of thirty years, it has been my privilege to perform and witness the making of a very large number of necropsies. Out of this vast number extending into the thousands, these two cases are the only ones that came directly under my immediate supervision.

It was also my privilege to see the specimen that was removed

from the case reported by Professor Halstead,[4] which makes a total of three cases seen in thirty years. In Professor Halstead's case the diagnosis was made by examining the fluid withdrawn from the peritoneal cavity. Professors Burt [5] and Steiner [6] both report cases diagnosticated by examining the fluid withdrawn from the peritoneal cavity. The difference between their cases and mine so far as the method of diagnosis was concerned, was that in their cases the diagnosis was made from the fluid withdrawn from the cavity of the peritoneum, while in my first case it was by directly puncturing the neoplasm in the liver. Dr. Steiner appends to his article a number of cases in which the diagnosis of carcinoma within the abdominal cavity was made by paracentesis abdominalis.

The credit for the actual diagnosis in my first case is due to Professor Brooks, as he passed the final judgment upon the material withdrawn from the neoplasm. It further establishes the fact that it is possible to make a correct diagnosis of tumors of the liver which are cancerous in nature, which before this was regarded as very doubtful if not impossible.

In the second case the symptoms led us widely astray, so far as locating the primary seat of the cancerous growth was concerned. The actual diagnosis being made only at the necropsy. It is another typical illustration of the absolute impossibility of making at all times correct diagnoses of pathological conditions within the thoracic and abdominal cavities, no matter how careful the clinician may be in his investigations.

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# ACUTE GASTRITIS

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The term gastritis has been often loosely used to include, in addition to inflammatory conditions of the stomach, a number of purely functional affections, in which the characteristic features of inflammation are absent. It should be applied only to those states of the gastric mucosa and musculature in which the latter features are present; in this restricted sense the term includes a large number of conditions.

Fleischer and Ewald describe the following varieties: (1) simple acute, (2) secondary acute, (3) purulent or phlegmonous, (4) toxic, (5) croupous, mycotic, parasitic, and (6) chronic gastritis.

Fleiner classifies the acute forms into (1) acute catarrhal, (2) toxic, (3) interstitial suppurative and phlegmonous, and (4) mycotic.

A. Pick describes the acute forms as (1) acute, (2) infective, (3) phlegmonous, (4) toxic, and (5) parasitic.

Penzoldt and Einhorn adopt a rational classification of acute gastritis as (1) simple, (2) phlegmonous, and (3) toxic; and I find this of considerable assistance in dealing clinically with gastric disorders.

Every temporary and passing gastric disturbance has no more real claim to be diagnosed as acute gastritis than every case of prolonged loss of appetite with eructations and coated tongue has to be regarded as chronic gastritis; and the more uniformity in conception and diagnosis of the several gastric ailments that obtains amongst clinicians, the better for the therapeutics of these affections and for the general advancement of this important field of medicine. All disorders, then, of gastric motility, absorption and secretion, as also of innervation and vascular supply, in which organic changes are absent, should be classed as functional, but great care should be taken in the diagnosis to exclude organic change.

It has been long known that every severe inflammatory irritation of the gastric mucosa produces an alteration in the gastric secretion, and further, that the impairment of one function rapidly involves that of another. Gastric secretion, for chemical and pathological study, may always be had for the trouble of withdrawing it; and it is to be regretted that so few avail themselves of the exact and comprehensive information to be thus obtained from it.

The lining of the stomach, in the strict sense, can hardly be called a mucous membrane, as it is lacking in mucous glands. The mucus of a healthy stomach is very small in amount, and is derived from the mucoid degeneration of the superficial columnar epithelial cells. These cells pass down into the alveoli of the peptic tubules and come into direct contact with the parietal cells, so that irritants affecting the surface cells will, according to their energy and length of time of action, more or less affect these sources of pepsin and hydrochloric acid. It is thus characteristic of the pathology of gastric digestion that the impairment of pepsin secretion is accompanied by the impairment of hydrochloric acid secretion, and vice versa.

It is not certain which function suffers first, but probably in most cases a derangement of secretion or of motility. If by ingestion of food which is already in a state of fermentation an acute gastritis has been induced, the reduction of hydrochloric acid furnishes an obstacle to the continuation of the normal chemistry of the stomach, and motility and resorption are immediately retarded. The subacidity leads to imperfect digestion of proteids so that only traces of peptone and soluble albumose are found in the vomit. Further, these undigested proteids remain longer in the stomach than under normal proteolysis, and this adds to the burden to be supported by the gastric walls, whereby the stomach fails to obtain that rest demanded for the digestion of the following meal. Again, under this subacidity more carbohydrates are converted into soluble starch, maltose, etc., than under normal acidity, and thus more ready food for bacteria is produced, whereby the four well-recognized forms of gastric and disordered fermentation are initiated, viz., alcoholic, acetic, lactic, and butyric. The active micro-organisms in these fermentations are severally and constantly introduced with the saliva. That form of excessive fer-

mentation most met with in the stomach is the lactic acid variety. It may here be pointed out that the above fermentations occur normally in healthy stomachs, but to a very limited degree. Immediately they cross this boundary they are accompanied by well-known symptoms, objective signs, and pathological findings.

The toxic products of this carbohydrate and proteid decomposition are irritants to the mucosa, and increase the already existing inflammation, which, on reaching a certain stage, is succeeded by an inflammatory œdema of the muscular layer, which effectually destroys the motility, and simultaneously throws out an alkaline fluid on the inner surface which neutralizes the last trace of hydrochloric acid. In addition to the lactic, acetic, and butyric acids formed from the fermenting carbohydrates, carbon dioxid and hydrogen are produced, and often in such quantities as to distend the stomach to an acutely painful degree. Peristalsis ceases, and further ingesta only add to the general gastric incompetence and distress. It cannot be too earnestly urged that a normal supply of hydrochloric acid is constantly required, not only as an integral factor in peptic digestion, but as an antiseptic and antifermentative, as also an active agent in the production of peristalsis. This mixing and triturating peristalsis is an essential stimulus to absorption and to the timely expulsion of the chyme into the duodenum. An intimate contact of the ingesta with the membrane is essential to normal stimulation and to continued secretion; hence in its absence the secretion of the oxyntic and ferment cells soon ceases entirely. Resorption is not only impaired by absence of intimate contact with ingesta, but by the fact that the epithelial surface, in acute gastritis, is covered with epithelial detritus and occasionally pus. These inflammatory changes affect very readily the rate, tonicity, quality, and quantity of the gastric blood flow.

The clinical picture is a manifold one, and only to be interpreted by the most careful study of the underlying causes.

In the majority of cases acute simple gastritis is produced by errors in diet—errors in quantity as well as in quality. Liquid or solid articles that have undergone fermentation will set up inflammation through the bacteria and toxins they contain. It is not always necessary for bacteria to invade the gastric epithelia. Decomposed vegetables, fish, meat, wine, beer, milk, or impure water

have been known to produce severe acute gastritis. Excessive ingestion of wholesome food can provoke the trouble, through mechanical distension and irritation, through overtaxing of the motility, and through a deficiency of the gastric juice, which last may be able to digest a normal but not an excessive quantity of food.

Acute gastritis has been known to follow the administration of 30 grains of sodium salicylate three times a day, large doses of quinine, and all metallic salts such as copper, antimony, arsenic and lead. Oil of sandalwood, copaiba, and cubebs have produced severe gastritis in susceptible patients. The psychic conditions of grief, terror, anger, and even excessive joy have given origin to the condition. The swallowing of very hot and very cold liquids under certain conditions of bodily health and external temperature, as also a countless number of mechanical causes, all lead to the same result. A singular case of acute gastritis occurred in a young man of 28 years of age through a blow from a cricket-ball, received over the stomach. Loss of consciousness supervened for a few minutes, and on recovery the patient vomited a meal which he had taken some two hours previously. Milk was administered later, which was in turn vomited; on testing the reaction, the vomitus was found to be distinctly alkaline. This patient was fed for four days on nutrient enemata, and made a good recovery in two weeks. Free hydrochloric acid reappeared at the end of eight days.

Acute gastritis has been produced experimentally in dogs by inducing fever; and Leube, Kussmaul, and others have found marked sub-acidity in the human subject suffering from fever.

I have found many instances of acute gastritis produced in several members of the same family by causes incompetent to effect the condition in normal individuals. Ewald supports this finding, and holds the view that certain families possess a distinct hereditary predisposition to the malady. It has been reported that an otherwise robust physician suffered from acute gastritis every time he ate oysters.

In infants, gastritis is produced at one time by a change in their milk, at another by continuation of the same milk. I have frequently seen the freshest cow's milk, duly modified, produce severe gastritis in children under a year of age, and the same infants recover completely in a short time when fed on a modified dried

milk. The sterility of the latter seems to be a most important item in the feeding of these cases. Acute gastritis in infants is accompanied by prolongation of the time that milk is retained in the stomach. When this time has been sensibly increased an entire change in feeding should be made, otherwise a vicious circle may be instituted.

Since uncomplicated, simple acute gastritis rarely ends in death, and since post-mortem auto-digestion exerts a disturbing influence on the gastric lining, comparatively few cases of such exudative inflammation have had their pathological anatomy thoroughly studied. In the few cases that have been examined by Ziegler, Laboulbene, Fischl, Delafield, Booker, Ewald and Ebstein, all these observers have found within 24 hours after death, hyperæmia of the mucosa, localized ecchymoses, swelling of the alveoli, augmentation of mucus, and infiltration of the superficial secreting cells with polynuclear leucocytes, nuclear extrusion and granular degeneration of certain of the oxyntic cells. Bacteriological examination of the secretion and superficial cells revealed streptococci, B. coli, B. lactis ærogenes, proteus vulgaris, and other organisms.

These changes are accompanied, in life, by fulness in the epigastrium, which is distended and painful to pressure, thirst, anorexia, offensive breath, and a tongue thickly covered with white fur, large and markedly indented. There may be acid eructations with greatly increased flow of saliva, and a burning pain at the epigastrium, which radiates either straight through to the back, or to the left hypochondriac region. There may also be painful contractions of the œsophagus, spasmodic yawning, and more or less continual raising of sour stomach contents. Taste is much disturbed, and diet is detested; or in a few cases a perverted craving for acid and salty foods may take possession of the patient. Palpitation of the heart, rapid and small pulse, general malaise passing into prostration, with profuse sweating, are found in a limited number of cases. Children, and nervous and less resistant adults, may occasionally suffer from delirium. I have found in a large number of cases of pronounced acute gastritis a combined frontal and occiptal headache, not relieved by posture or food, and frequently aggravated by vomiting.

It will be perceived that these symptoms arise directly from

the stomach or reflexly from the central nervous system, which latter suffers intensely at times from gastric absorption of bacterial toxins. If nausea ends in emesis, food may be rejected that has been eaten many hours previously, very imperfectly digested or unchanged, and covered with thick and tough mucus. Frequently vomiting continues after the stomach has been emptied, and bile, mucus, and blood may be ejected under great retching and pain. Chemical analysis of the vomit demonstrates lactic, butyric, and acetic acids, where carbohydrates have been recently ingested; but the most characteristic and important condition is the utter absence of free hydrochloric acid, the origin of the irregular fermentations in the gastric contents. About fifty per cent. of cases show a greater or less rise of temperature. In a few cases 104° F. or 105° F. may be reached, and this temperature may greatly obscure the diagnosis. In cases unaccompanied by rise of temperature there is little or no difficulty in diagnosing the condition, especially as the exciting cause is more or less apparent. But febrile forms may be confounded with the early stages of typhoid fever, and during the first three or four days it may be impossible to differentiate one from the other. Widal's test is useless until the second week, and Ehrlich's diazo reaction has, I must confess, in my experience no value. It is well to observe von Leube's dictum in these cases, namely, to think of other sources and causes of trouble in all cases with high fever, before settling upon gastritis. The element of time is of import here, as simple acute gastritis rarely lasts longer than four days. In typhoid fever the mode of rise of the temperature and the condition of the spleen, are for the most part distinctive. The absence of splenic enlargement and the abrupt rise of temperature are fairly characteristic of acute gastritis, but the experienced and wise practitioner will not be carried too far by these, as splenic enlargement is not invariably met with in typhoid, and a few cases exhibit a rapid rise of temperature.

The treatment is (1) dietetic, and (2) medicinal. It may seem a platitude to state that acute inflammation of any organ is best treated by rest; but in the case of the stomach, the most overworked, perhaps, of all organs, rest is the first necessity. Total abstinence from all solid food and the least possible fluid for a

period of 36 to 48 hours is curative in a large number of cases. If great thirst exists a little ice to suck is all that is necessary. If after 36 hours symptoms have not abated rectal enemata perform most excellent service, and in most patients this type of feeding can be prolonged for a few days with the happiest results. The following enema I have found very suitable: One hour after washing the rectum, inject

250 grams of fresh milk
2 yolks of fresh hen's eggs
1 teaspoonful table salt, and
1 tablespoonful red wine.

This may be administered three times in the 24 hours. Acute gastritis should be treated without drugs.

In a few cases, especially in children, where emesis does not occur readily at the outset, Ewald and Boaz recommend an emetic of ipecacuanha. I prefer to do without emetics. If resort must be had to any drug let it be calomel. In some cases of pronounced nausea this salt acts as a gastric sedative. Half a grain of calomel, administered hourly until purgation, in some cases is very effective, but it should never be given until the second day of the illness. Intense pain and incessant retching are best met by hypodermic injection of one-quarter grain of morphia. Where, during the first day, emesis has not been effective in acute cases, lavage of the stomach should always be performed, so as to get rid of fermenting food stuffs. Purgatives should not be administered, with the sole exception of calomel, and it always after lavage.

Where persisting vomiting exists, in addition to morphia hypodermically, one may give ice to suck and try mustard plasters on the epigastrium. If these fail, a mixture of

| | |
|---|---|
| Bismuth salicylatis | gr. x |
| Cocain hydrochlor. | gr. ½ |
| Menthol | gr. ii |
| Aq. camp., q. s. | ℥iss |

may be given every two hours until the patient is relieved. It may be pointed out, however, that in my experience, washing out the stomach and lower colon and rectum, with a weak solution of boric acid and thymol, without any swallowing of drugs, is thoroughly effective in 99 per cent. of all cases of severe vomiting.

# THE SALIENT FACTORS IN THE ESTIMATION OF RENAL DISEASE

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The marked discrepancies which frequently exist between the clincial diagnosis of kidney diseases and the post-mortem findings in the same cases have necessitated a readjustment of standards, with a placing of changed values upon certain clinical data. A few decades ago the presence of albuminuria was regarded as pathognomonic of organic renal diseases, but we now admit that both albumin and casts may be present without gross renal lesions and that serious organic renal disease may exist without either albumin or casts. In fact, varying quantities of albumin, with or without casts, may be present in the urine for considerable periods of time, entirely compatible with seemingly perfect health.

Regarding the relative insignificance of casts in the urine of individuals past middle age, Herrick, in Nothnagel's Encyclopædia, poetically observes that, "It is doubtful if in many of these cases the stray cast means much more as regards health than the appearance of wrinkles on the face or a few gray hairs on the head as one advances in years;" or, as Osler puts it, "A trace of albumin in a man over forty, with or without a few hyaline casts, is not of much significance, except as an indication that his kidneys, like his hair, are beginning to turn gray with age."

## SIGNIFICANCE OF ALBUMINURIA

The more delicate and sensitive the test, the more frequently is albumin found in healthy urine. Spiegler[1] by means of exceedingly sensitive tests has shown that traces, both of nucleo-albumin

[1] Centralbl. f. klin. Med., 1893, No. 3.

and serum-albumin occur very often in normal urine. Morner has proved conclusively [2] that serum albumin is a normal constituent of urine, in quantities of 22 to 78 mgm. to the liter. In fact, with the refinement of methods, many substances, which have at one time been regarded as abnormal constituents of urine, are now recognized as present in small quantities, but vary under certain physiological conditions, *e.g.,* sugar, oxalic acid, fat. indican and urobilin.

If albumin in small quantities is a normal constituent of urine, the quantity may vary under physiological conditions, and it becomes difficult to determine boundary lines—between the physiological and the pathological. Numerous terms have been used to describe the supposed causes of physiological alubuminuria—such as orthostatic, muscular, simple, persistent, neurotic, postural, digestive, cyclic, adolescent—all of which are an effort to attribute causation. Hard muscular labor or exercise is known to cause transient albuminuria. Recently I made some interesting investigations in ten basket-ball players ranging in age from 18 to 24 years. The urine passed by each before a hard game was absolutely free from albumin and casts, and after an hour and a half of vigorous exercise four of the ten showed faint, but distinct traces of albumin and two others gave very suspicious but hardly pronounceable traces. No casts were found in any specimen. Sexual factors, such as coitus, masturbation, pollutions, and without doubt, various psychical stimuli contribute their quota, although I am inclined to believe that many of these cases are spurious, not true albuminuria, but due to an admixture of seminal or prostatic fluid. Following the suggestions of Ballenger, I have within the last four months examined the urine of fourteen cases with prostatic inflammation, embracing acute, sub-acute and chronic forms. I also have records of seven cases of chronic posterior urethritis with prostatitis. In the unfiltered morning urine of all I found distinct traces of albumin—due in most instances to pus cells, spermatozoa, or other organic matter—extra-renal in origin, whereas urine passed later in the day contained no traces. In three prostatics with hypersecretion I found traces of albumin in the *filtered* urine. Without

[2] Skandin. Arch. f. Physiolog., 1895, vol. vi.

doubt the over-secretion seeps into the bladder and thereby causes confusion.

I have never failed after massaging the prostate, when acutely or sub-acutely diseased, to find in the urine immediately passed, from faint to marked traces of albumin, and this in many instances with the filtered urine. Such cases are false albuminuria, but no doubt contribute their quota to the so-called physiological varieties.

*The true physiological varieties* are most probably due to circulatory changes in the kidney, which may be of transient duration. The etiology of postural or orthostatic albuminuria has been discussed at considerable length in recent articles by W. V. Leube,[3] C. L. Mix [4] and Wm. H. Broadbent.[5] This form occurs chiefly during adolescence, and it would seem to bear some relation to the unstable circulatory system at that age, together with the profound efforts at readjustment in the nervous and sexual systems. Le Noir, Kuttner and Sunderland have found movable kidneys in about thirty-five per cent. of the cases of so-called albuminuria of adolescence. A general splanchnoptosis has been noted by Kuttner and the consequent diminution of abdominal pressure may be a factor in the circulatory variations in the kidneys, which without doubt may give rise to albuminuria. Many theories have been offered as to the place in the kidney where the escape of albumin occurs, but in the majority of instances the albumin evidently transudes from the blood into the urine, through the glomerular tufts. However, in a limited number of cases where there is a destruction of the epithelium lining the tubules, there may be an albuminuria, but it is supposed that under normal conditions the epithelium lining the uriniferous tubules absorbs, rather than excretes, certain albuminous bodies excreted through the glomeruli.

### PATHOLOGICAL NON-RENAL ALBUMINURIAS

When alubumin appearing in the urine becomes pathological and of real clinical importance, it must first of all be *persistent.* Albumin appearing in one urinary examination and absent in all subsequent tests is of little significance as a diagnostic factor. Albu-

[3] Deutsche med. Wochenschrift, 1905, vol. iii.
[4] Am. Jour. Med. Sc., Aug., 1904.
[5] Deutsche Archiv f. klin. Med., Sept., 1905.

min which *persists* for months and years is always suspicious if not an absolute pronouncement of organic disease. There may be merely a chronic circulatory disturbance, which may ultimately give rise to organic changes in the kidney itself, and the renal parenchyma may become the seat of inflammation or degeneration. Then, too, a limited number of cases presenting albuminuria would seem to be due to a blood dyscrasia, in which there may exist some abnormality in the forms of albumin present in the blood. Such forms of albumin, because they differ in their properties from the serum albumin and serum globulin or normal blood, may make their way into the urine through a perfectly healthy kidney. This hæmatogenous class, strictly speaking, should also include the toxic varieties, due both to inorganic poisons and to the organic toxins of infectious disease.

Gerhardt [6] described a febrile albuminuria associated with the acute exanthemata, diphtheria, influenza, typhoid, pneumonia, rheumatism and erysipelas occurring during the fever and disappearing with it. Von Leyden, however, considers this a mild form of infectious nephritis, which however, may persist and give rise to a true parenchymatous nephritis.

There is a border-line class of cases with certain blood involvment and occasional demonstrable epithelial change in the kidney structure. This form comprises the leukemias and pseudo-leukemias, pernicious and profound secondary anæmias, scorbutus and the various forms of icterus.

Another class of cases of albuminuria without discernible alteration in kidney structure is associated with various nervous disorders, such as hysteria, neurasthenia, epilepsy, and migraine. The cause may here lie in the sympathetic nervous system, which governs the vaso-motor and thereby the renal circulation, or it may originate through disturbances in the centres higher up. Perhaps more refined methods of examination may reveal a co-existent minute renal epithelial alteration in many of these cases.

### ALBUMINURIA WITH RENAL LESIONS

Once settled that albumin is of renal origin in a given case, the relationship of this albumin to nephritis becomes a question of

[6] Deutsche Archiv. f. klin. Med., v, 1868, p. 212.

paramount importance. Many excellent authorities consider every albuminuria pathological; others admit frequent instances of a purely physiological or functional appearance. It would seem that Osler in his last edition has summarized the so-called functional albuminurias in a most sane manner: "The presence of albumin in the urine, in any form and under any circumstances, may be regarded as indicative of change in the renal or glomerular epithelium, a change, however, which may be transient, slight and unimportant, depending upon variations in the circulation or upon the irritating effects of substances taken with food or temporarily present, as in the febrile states." But as albuminuria is only one symptom of kidney mischief, and as Thos. Fuller says, "Reasons drawn from the urine are as brittle as the urinal," let us consider other criteria which are of distinct value in the estimation of renal mischief.

Several investigators have recently startled us with the amazing discrepancies between the clinical diagnosis and the pathological findings in the same cases as found by men of undoubted skill, and we must admit that our present methods for the diagnosis of kidney disease are sadly inefficient, not to say, inaccurate.

Cabot[7] in a masterly comparison of clinical and post-mortem data concludes that there are many cases of acute glomerular nephritis which cannot be recognized by any of the methods of examination known to us; that in some cases of subacute and chronic glomerular nephritis our diagnostic resources are likewise at fault; and that the attempt to estimate the anatomical condition of the kidney by the measurement of albumin and the search for casts is fallacious in the extreme. Dr. Chas. P. Emerson of Johns Hopkins in a study of over 1000 cases with 500 autopsies confirms the conclusions of Cabot.

### THE SIGNIFICANCE OF URINARY CASTS IS AN UNSETTLED PROBLEM.

Casts are moulds of the uriniferous tubules and consist of a coagulable substance segregated from the blood, which on contact with the secreted urine, solidifies, embodying in their molds, whatever the tubule may contain—loose epithelium, granules, pus or blood cells. As they contract, they become loose and are forced

[7] Journal A. M. A., March 18 and 25, 1905.

out by the urinary flow from behind. The true origin of the coagulable substance is still an unsettled question. Hyalin casts are probably the primary form and are the basis of all other forms by incorporation or accretion. They are peculiar to interstitial nephritis, but are likewise present in practically all so-called functional disturbances.

One fact that leads us to believe that hyalin casts are the basic form is that hyalin casts frequently occur alone, but other forms never do. Hyalin casts are present in the majority of persons beyond forty years of age.

Granular casts, though an evidence of degenerative changes in the tubular epithelium, are pathognomonic of no one condition. Epithelial casts are present in renal hyperemias, both active and passive, and in desquamative nephritis, which comprises the acute and chronic parenchymatous forms. Waxy, fatty, blood, pus and mixed casts and cylindroids are names applied to various forms which may be found in the urine. Fatty casts or hyaline casts covered with fatty epithelium evidence a degeneration of cellular structure; blood casts or other casts with blood cells attached would indicate a parenchymatous hæmorrhage; the presence of leukocytes or pus cells in granular casts or embodied in other casts must signify an inflammatory condition.

From the presence of a few casts, of one type or another, we have been accustomed to diagnosticate some form of nephritis—if granular, a parenchymatous, if hyalin, perhaps an interstitial variety. The *quantity* and the *persistence* are the most important data. With a persistent quantity of any variety organic disease is evident. But the presence of occasional casts—be they hyalin, granular or epithelial—may mean only a minute embolism or thrombosis of some arteriole with a consequent ischæmia or anæmia, or a disturbed balance of endosmosis and exosmosis in some one or few uriniferous tubules. Through nature's prompt recuperative methods normal conditions are quickly restored, and there is a prompt and permanent disappearance of the suspicious cast. I would emphasize then, that not the mere presence, but the *persistence* and the *quantity* of urinary casts are indices of organic mischief—and the type of cast is merely of differential value.

It is quite evident that the mere daily loss of quantities of

albumin or the concomitant presence of casts may not seriously affect the health; but the total quantity of fluid excreted and the total amount of solids eliminated, as indexed by the specific gravity of the twenty-four-hour specimen must remain within normal bounds.

The kidneys are primarily organs for the elimination of water, the products of metabolism and other excrementitious material, and *the index of renal function is to be found not so much in the quantity of abnormal products, such as albumin and casts, that are eliminated, as in the preservation of the normal ratio in the excretion of its normal products.*

The evidences of true renal insufficiency are recognized symptomatically in dropsy, uræmia and increased vascular tension with consequent cardiac hypertrophy.

Renal dropsy is similar if not analagous to that observed in valvular disease with broken compensation, but must not be confused with the anasarca which develops in the later stages of many diseases due to enfeebled heart action which gives rise to a venous congestion. Whereas dropsy appears late in these conditions, *renal* dropsy generally occurs early, though its manifestations may be slight. The skin about the eyes, over the tibia, and ankles shows the first signs. Later the œdema is of a more general nature, appearing both in the subcutaneous tissues and the serous cavities. It is then generally complicated in its etiology by increased vascular tension with cardiac hypertrophy, venous stasis, and perhaps broken compensation. The true renal dropsy is most extensive in acute nephritis and disappears or at least diminishes with the stage of contraction. The chief evidence of secondary contraction lies in the increase of vascular tension which necessitates more forceful ventricular contraction and consequent hypertrophy with an accentuation of the aortic second. In many instances the hypertrophy does not keep pace with the increased vascular tension and ruptured compensation occurs, which then increases the anasarca.

In renal insufficiency, the retention within the blood of excrementitious substances, largely cleavage products of proteid metabolism, gives rise to uræmia, a condition of grave import, and characterized by the familiar syndrome of drowsiness, headache, dizziness, vomiting, impairment of the vision, convulsions and coma.

*The urinary evidences* of renal insufficiency are evidenced in the measurement from day to day of the total 24-hour quantity, and the specific gravity of the same, which weighs in a fairly accurate manner the amount of solids eliminated. Cabot suggests determining whether and to what extent a kidney is able to secrete a dilute urine after profuse ingestion of fluid, or a concentrated urine when liquid is withheld.

Much work remains to be done in the study of renal function and the elaboration of technic for the estimation of renal efficiency. Unfortunately, the urine only partially and at times very inaccurately mirrors the pathological status with which we have, therapeutically, to deal.

We must conclude, therefore, that a frequent source of error in the estimation of urinary findings is the admixture of albuminous substances from extra-renal sources.

Though the presence of albumin and casts is always of significance, the most reliable prognostic data lies in the determination of renal function as regards the maintenance of a *normal* ratio of excretion of *normal* urinary constituents, through the measurement of the 24-hours quantity and its specific gravity.

The appearance of increased vascular tension with attendant cardiac hypertrophy and an accentuated aortic second sound, speak volumes for the existence of interstitial contraction in the kidneys.

There seems to be a brighter day dawning in kidney work, and the fundaments of achievement will not lie in speculative pathology but in the study of *function* with a close regard for the preservation of *normal ratios of excretion,* and *less regard* for the significance of abnormal constituents in the urine.

# GENERAL ABDOMINAL ENLARGEMENT, WITH SPECIAL REFERENCE TO THE HEPATIC CIRRHOSES *

BY MARK A. BROWN, M.D.

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GENTLEMEN: I have to present to you this morning two patients afflicted with apparently general abdominal enlargement. The term "general" is used advisedly, as we frequently encounter distensions distinctly localized to some definite portion of the abdomen. For instance, some of you may remember having seen in the wards, a few days ago, a man with a localized fluctuating swelling most marked in the left iliac region, though following the course of the colon. This was found on post mortem, as was thought in the wards, to be due to stricture of the sigmoid flexure, secondary to carcinoma of the liver. Cases of this sort are, however, among the most difficult of diagnosis and at this time we will confine our studies to the more simple generalized enlargements.

The first patient to whom your attention is called is this old man, and when his abdomen is bared you are immediately struck with its enormous distension; so bulging, in fact, and apparently so tense that it would seem impossible for further enlargement to take place. To this is added a marked protrusion of the umbilicus, umbilical hernia, probably dependent upon an increase in intra-abdominal pressure. There is also present, as you can readily see, a peculiar sheen or glossiness to the skin of the abdominal wall, dependent upon the same increased intra-abdominal pressure. Even from your seats you can see extreme dilatation of the superficial veins of the chest and abdomen; this is not particularly marked around the navel. You will note that while there is some bulging in the flanks, this is not especially marked for reasons that will presently appear. The abdominal enlargement is symmetrical.

Now, in contra-distinction to the huge size of the abdomen, direct your attention to the thinness of the chest and the emaciation of the

* Clinical Lecture delivered at the Cincinnati Hospital, March 12, 1907.

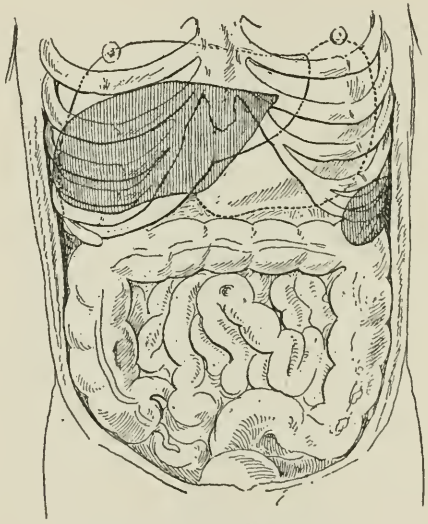
arms. The lower extremities, particularly below the knee, apparently do not share in this emaciation, which is explained by the fact that they are œdematous—that is to say, filled with fluid, a point easily demonstrated by their retaining for a considerable time their "pit" on pressure. The face is thin, the eyes watery, the skin sallow, and there are small dilated veins in the cheeks and about the nose. There is a faint yellowish discoloration of the ocular conjunctivæ, hardly deep enough to be called jaundice. On both these latter points you will be able to assure yourselves when you come down to examine the patient. The skin of the entire body is, as you see, sallow, but there is no icterus as we understand the term. So much for inspection.

On palpation we naturally, in a distension so marked, search for and easily obtain the physical sign known as fluctuation. This is elicited by placing the hand low down upon one flank and tapping lightly with the tip of the finger on the opposite side; fluctuation, if present, reveals itself by the transmission of a wave to the palpating hand. The presence of this sign is, as you know, indicative of fluid. Except that we find that the abdominal wall is quite thin and exceedingly tense, palpation in this patient is otherwise negative. This tense condition effectually prevents palpation of the liver and spleen. Percussion in the right nipple line with the patient in the recumbent position reveals a liver dulness beginning somewhat higher than normal, the note becoming absolutely flat before reaching the costal border and continuing so downward to the ilium. In the median line, while we encounter above a small area of dulness and flatness, this is soon succeeded by a note markedly tympanitic. The entire left flank is flat. We find then that with the patient in the recumbent position there is a considerable area of tympany in the centre of the abdomen, the sides preventing flatness on percussion. Now, placing the patient upon either side, we find that the percussion note on the side uppermost is tympanitic, while that over the portion of the abdomen previously tympanitic is flat. This sign of the phenomenon of movable flatness is a positive indication of the presence of fluid, even if we had not been made aware of it by the fluctuation wave.

The history is briefly as follows: The family history is negative. Patient himself denies venereal diseases, admits alcoholism, from

twelve to fifteen glasses of beer daily and one glass of whisky daily for the past twenty-seven years. Up until the middle of January of this year he was apparently entirely well. At that time he found that upon stooping he was seized with rather severe abdominal pain most marked in the region of the umbilicus. Soreness then became more or less constant, with acute exacerbations of intense sharp pain at and below the navel over a region about the size of the two palms. He noticed for the first time some swelling of the abdomen and feet, and this condition has steadily increased. He has never vomited, bowels have been kept open with various cathartics. For the five or six days previous to his entrance to the hospital, February 8th,

FIG. 1.



Area of liver dulness in Case 1.

he says that his stools have been black. Examination of the heart and lungs revealed nothing abnormal. The abdomen was about as has been outlined to you, though the distension at the time of his entrance was not so great. Urinalysis, acid, amber, clear, specific gravity, 1024, no albumen, no sugar, no casts; a few pus cells. One week ago, the usual treatment of vigorous saline catharsis having been of no avail, the abdominal fluid was aspirated, and 17½ pints of clear, straw-colored highly albuminous fluid removed to his great relief; however, you see how rapidly the fluid has accumulated.

With the withdrawal of the fluid we were able to outline the liver by combined percussion and palpation. As you will see from the diagram (Fig. 1), it is very irregular in outline and decidedly diminished in size. Toward the median line, anteriorly, the edge of the liver extended at the point of its greatest convexity, fully 1½ inches below the costal border, at which point, on account of the thinness and relaxation of the abdominal wall, the irregular, uneven, granular surface could be readily felt. In the right nipple line and toward the right flank the vertical diameter of the liver was markedly diminished. The spleen was enlarged to percussion and palpation. These points we cannot demonstrate to you to-day, owing to the re-accumulation of the fluid. The temperature since he has entered the hospital has never been above 100° and has been as low as 97°, reaching this minimum usually in the early morning. With the history of pronounced alcoholism over a long period of years, with accumulation of ascitic fluid, which when removed reveals a contracted, irregular, hobnail liver and enlarged spleen, with the marked dilatation of the superficial veins of the chest and abdomen, with absence of disease of the heart and kidneys, we have little difficulty in making a diagnosis of atrophic cirrhosis of the liver.

I will not at this time go into the pathology of the affection, but will next direct your attention to our second case of abdominal enlargement, the history of which is as follows: The family history has no particular bearing on the case. Personal history: has had ordinary diseases of childhood, lead colic about fourteen years ago, has followed occupation of musician since that time. Admits "eczema," denies venereal diseases. Alcohol has been taken in excess, for the patient admits an average of over twenty glasses of beer and eight glasses of whisky per day for the last eight years and to a somewhat less extent for the previous seven years; he has drunk to excess for a period of at least fifteen years. Chews about a package of tobacco daily; does not smoke. About eight years ago he weighed from 150 to 160 pounds and his abdomen was thin and flat. He has steadily increased in weight until now he weighs 275 pounds. For the last three years his feet have swollen occasionally, and for the last year he has suffered from dyspnœa, at times amounting to orthopnœa; particularly has this been the case at night. Of late he has complained of weakness in the arms and legs, especially

of the latter, the condition becoming steadily worse, so that at the time of admission he was unable to walk even with assistance.

These symptoms, together with a slight swelling of the feet and a severe cold he had contracted, were what compelled him to apply for hospital treatment. Temperature on admission, 100.4°; pulse, 120; respiration, 38. Physical examination: The principal point noted about the face at that time was a slight jaundice detected best in the conjunctivæ. There was also some distension of the venules of the cheeks about the nose. Chest: Apex beat of the heart neither seen or felt; no heart murmurs; sounds of heart not distinct except second pulmonic, which is short and sharp. Subcrepitant rales heard at the base of the left lung posteriorly; otherwise the lungs are negative. Abdomen is very large; while he is on his back, it is tympanitic in the left flank, but there is dulness on the right side almost to the anterior superior spine of the ilium; this on palpation is found to be the liver; the edge is hard, firm and smooth. Veins of the abdomen and chest somewhat enlarged. Extremities: Wrist drop and foot drop, latter most marked, right and left. Some œdema of feet. Urinalysis: Urine, dark, reddish-brown, turbid, alkaline, specific gravity, 1026; slight amount of albumen, no pus or casts, amorphous phosphates; bile marked. Cutaneous symptoms: Copper-colored (syphilitic) eruption on lower abdomen, legs and arms; syphilitic psoriasis on left forearm; on both legs between knee and ankle, skin greatly discolored over a large area, and several ulcerations present. Skin over whole body slightly jaundiced. His age is 36. These were the notes taken on his admission to the hospital, December 22. Since that time, under rest in bed, abstinence from alcohol, moderate catharsis, and the use of mercurials, locally and internally, and of the iodide, he has gradually improved. His wrist drop has shown marked improvement, the foot drop very little; the swelling of the feet has disappeared, as have the eruptions on the skin and the ulcers of the legs; the jaundice, after deepening a little, has slowly lessened in intensity. The liver at its lowest point is about three fingers' breadth from the ilium, and there is, as you can hear, a well marked tympanitic note over this intervening space.

On examining this abdomen we find in comparison with the first case that it sags markedly at the flanks. On palpation we find

that the abdominal wall is extremely lax, so much so indeed that if we place a hand in each flank and bring them with some pressure toward one another in the median line of the abdomen we find that the great thickness of this wall, some three or four inches, is readily palpable. On attempting fluctuation, we find that a light tap, sufficient to bring out the sign in the first case, here elicits no response; in this patient a heavy blow will bring a faint response on the opposite side. Placing this man on either side does not change the character of the percussion note found on that side when he was lying on his back. There is no accumulation of fluid in the abdomen.

The enlargement of this abdomen is then for the most part due to an accumulation of fat in the abdominal wall, a not unlikely place for it to form. The temperature has been irregular, ranging between 96° and 100°, never above 101°, and running often for several days practically normal; it is usually lowest during the early morning hours. From the history of this patient, particularly that of excessive beer drinking, rapid accumulation of fat, multiple neuritis as shown by foot and wrist drop and other symptoms characteristic of this affection; from the absence of symptoms pointing to severe organic changes on the part of heart, lungs or kidneys; from the physical examination of the liver, large, firm, smooth, regular in outline, not sensitive to manipulation; from the faint jaundice and dilatation of the veins of the chest and abdomen (not nearly so marked in this patient as in the one first presented); from the absence of cachexia or suppuration, we have no difficulty in making a diagnosis of an enlarged, so-called fatty liver.

Indeed, we can go still further with this history of slight jaundice, venous dilatation and excessive alcoholism, especially the drinking of beer, and say that there is a certain amount of cirrhosis mingled with the fatty deposit, a cirrhosis with enlargement; not a biliary cirrhosis, because it is not likely that with this slight jaundice the biliary radicles are involved to any great degree. I do not believe that syphilis plays any great part in the production of this man's symptoms. While we can obtain no history as to the initial lesion, the character of the eruption indicates a secondary rather than a tertiary stage of the disease. The leg ulcers are not typically nor necessarily specific. That he has improved under

treatment does not mean that the improvement must be ascribed to the anti-specific treatment; rather indeed does it depend upon absolute rest in bed, regulation of diet, total abstinence from alcohol and free action of the emunctories.

Here then we have two cases of general abdominal enlargement, one dependent upon an intra-peritoneal accumulation of ascitic fluid, the other for the most part upon a deposit of fat in the abdominal wall. In both there is a serious involvement of the liver, though in the former patient this involvement is of a much graver character. The rapid accumulation of fluid after tapping, the smallness and deformity of the liver, cannot but incline us to a most unfavorable prognosis. He has been advised to submit to the so-called operation of Talma, by which an attempt is made to relieve the obstructive symptoms of the cirrhosis by establishing a collateral circulation. In this operation the abdomen is opened, the fluid allowed to drain away, the anterior surface of the liver, spleen, parietal peritoneum and intestines are roughened by being vigorously rubbed with gauze, and finally the omentum is attached to the parietal peritoneum of the anterior abdominal wall by sutures; it is hoped by this procedure that adhesions will be formed by means of which a collateral circulation may be established. Collected statistics of this operation show almost ten per cent. of recoveries which for a treatment of last resort upon a patient in a state of great mal-nutrition, is not discouraging. You will understand, of course, that the improvement is only temporary, that it has not the slightest effect upon the cirrhotic tissue within the liver; patients, however, who seemed to have been speedily doomed have under the operation lived for two or three years in comparative comfort. This operation our patient has steadily declined.[1]

Almost without effort on our part the trend of the lecture has been toward hepatic cirrhoses, the underlying pathology of both our patients being not dissimilar in that both depend upon excessive alcoholism, and in both there is in all probability an increase in the connective tissue in the external and intermediate zones of the hepatic lobules. Just why in the one case there has been an excessive accumulation of fat within the liver with comparatively little increase in the connective tissue and little or no cicatricial

[1] Died April 15th, 1907.

contraction of the same, while in the other there is no fat increase, great increase in connective tissue at the expense of essential liver cells, and cicatricial contraction sufficient to cause great deformity, it is impossible to say. Numerous theories have been advanced with which I will, however, not burden you; one clinical fact has, however, been repeatedly observed: the enlarged, fatty cirrhotic liver is the one most frequently observed in alcoholics whose potations consist principally of malt liquors, while the imbibers of spirits seem to be most commonly afflicted with the atrophic form.

As has been told you on previous occasions cirrhotic changes in the liver are by no means infrequent and many causes may be operative. One of the most frequent of these etiological factors is organic heart disease. Remember how very common an affection is organic disease of the heart. Remember, too, that the majority if not all the cases of heart disease are sooner or later attended with marked changes in the liver. With these two points in mind you will have some idea of the frequency of liver involvement of this type. You will recall from previous lectures that there exists dilatation or hypertrophy of both of the various cavities and walls of the heart in insufficiency or stenosis of its valves; that the left side of the heart is more capable of these compensatory changes than the right; that with the failure of the right heart, broken compensation, if you will, serious symptoms on the part of other organs than the heart ensue. At this stage, indeed for a considerable period before, there has been stagnation in the hepatic veins due to inability on the part of the inferior cava, into which these veins run, to empty itself thoroughly.

You will remember that the hepatic veins are formed by the sublobular and they in turn by the intra-lobular veins of the liver, the latter being situated at or near the centre of each individual lobule. Damming back of the blood in the inferior cava then manifests itself by stagnation in the liver, a condition known as passive hyperæmia or chronic congestion of the liver, which, as has been intimated, is to be expected in all cases of valvular disease of the heart of long standing. A liver of this kind is, particularly in the earlier stages, considerably enlarged, and the congestion of the central vein of the lobule as contrasted with the surrounding paler zone, brings out a beautiful lobular mottling to which has appro-

priately been given the name, "nutmeg liver." As time goes on more or less pressure-atrophy of liver cells, particularly those surrounding the dilated, engorged central vein, ensues and new formed connective tissue takes the place of the essential liver cells. This may, if continued sufficiently long, eventually bring about a condition of cirrhosis known as cyanotic induration, due to the inevitable contraction of the newly formed connective tissue, in which the liver becomes reduced in size, becomes somewhat granular, and offers resistance to the knife on section. This is also known as secondary cirrhosis, and has its beginning from the onset of the period of chronic congestion. It is only when the process has proceeded to a very considerable degree that the liver becomes diminished in size.

The patient that I now present to you has no doubt a "nutmeg liver" in the stage of enlargement. He is 58 years of age, and for many years has led a life of exposure and neglect. Alcoholism and venereal disease seem to have played no part in the production of his present condition. He also states that he has never had inflammatory rheumatism. The duration of his illness, as far as he is aware, does not exceed six months, and has manifested itself by steadily increasing shortness of breath. He has also had marked œdema of the feet and legs, and for the relief of all these symptoms he had applied for hospital treatment. His examination on entrance revealed organic heart disease with gravely ruptured compensation. Under absolute rest and the careful use of digitalis he has steadily improved, and now, as you see, is able to go about in comfort. His heart's action has become regular, and we are now able to make out well marked aortic and mitral regurgitation. In addition, we find on auscultation in the examination of this patient, that there is a murmur, systolic in time, heard at the lower end of the sternum and transmitted well to the right and upward. I will also call your attention to a positive (systolic) pulsation in the jugular veins. We are also able to detect on examining him in the position of Ewald (patient sitting in bed with knees drawn up, head leaning backward and resting on shoulder of examiner, who sitting behind patient supports him and at same time is able to reach around and palpate abdomen in front) a systolic pulsation in the greatly enlarged liver. These three symptoms are all dependent upon the

same cardiac lesion, tricuspid insufficiency, a lesion itself as a rule relative, and resulting from mitral disease. The pulsation on the part of the veins of the neck and of the liver is readily explained: The right auricle is unable to hypertrophy to any degree to compensate for the leakage in the right auriculo-ventricular valve, so that enormous dilatation of this chamber ensues with damming back of blood in both cavæ. Dilatation of these vessels now takes place, the valves of the veins in turn become incompetent, so that with each systole of the heart there is communicated a pulsation to the stagnated columns of blood in the cavæ. It is needless to say that this condition is an exceedingly dangerous one and that complete failure of compensation in cases of this character is but a matter of a very short time.

We have in the wards another case of probable cirrhosis of the liver in which the syphilitic poison has played the principal role, that I had hoped to present to you this morning, but the lateness of the hour will make it necessary to hold him over for another meeting.

# Surgery

## OBSERVATIONS ON THE INOCULABILITY OF TUMORS AND ON THE ENDEMIC OCCURRENCE OF CANCER *

BY LEO LOEB

When I was asked about twelve days ago, to read a paper to-night, I intended to make a small, quite unpretentious communication, giving a few observations and experiments on tumor-inoculation that I have made in the course of the last four months; but when, a few days later, I heard that the paper was to be discussed by some distinguished surgeons and pathologists, and that I was expected to speak somewhat longer than the usual time allotted, I saw that I must change my plans, it being too late to change the program, so, I had to enlarge the scope of my remarks and give a brief outline of some of the work done in the last seven years in the experimental investigation of tumors, instead of reporting a few experiments, I myself have carried out recently. After an interval of several years, I obtained, only six months ago, the opportunity of resuming my work; I will not try to go much into details, but rather to discuss some of the tendencies of cancer-investigation at the present time.

I wish to say in the beginning that I have no startling announcement to make. The "cause of cancer" has not yet been discovered; but I do not, therefore, agree with those that, without much hesitation, condense their final conclusion into the short statement that we know nothing, nothing at all, about cancer. Such a statement is not very encouraging for those that have given their energies to this work for some time; and what is more, I do not believe

* An address read before the Pathological Society of Philadelphia, April 11, 1907.

it is in accordance with the facts. We have learned something about cancer; and, much more than our actual achievements, we see the road clear for future work. We see problems on all sides, problems whose solution can be attempted successfully and that present outlooks into new fields. That is the difference between the conditions now and as they existed eight or ten years ago. There is now a feeling of hopefulness among the workers in this field that was not present until quite recently. In Germany, France, England, and Russia, new institutions for the study of cancer have been founded in the last few years. In America which did not lag behind in this respect, Boston, Buffalo, and New York have now special laboratories for the investigation of cancer; and a steadily increasing number of investigators are devoting their energies to this work.

What has brought about the change? The increase in the number of cancer cases, which, as some investigators believe, exists? Hardly. Such an increase is far from being proved. I do not think I shall be far from the truth, if I state that the generally awakened interest in cancer is due to the opening up of a new method of investigation—the experimental method. If I speak of the experimental method as a new one, I, perhaps, do not do full justice to the splendid work done by Hanau and Morau almost twenty years ago. The former transplanted cancer (a squamous epithelioma) in rats; and Morau, a carcinoma in white mice. This work proved that tumors can be transplanted into other animals. Hanau made very careful microscopic examinations of his transplanted tumors, and Morau made very interesting observations on the susceptibility of different strains of mice to the inoculation with carcinomatous material. These efforts, however, remained isolated, for pathologists were not yet prepared for this method of work. I may illustrate this:

About fourteen years ago I had the privilege of studying under Hanau, and the opportunity of speaking freely with him about problems in pathology; but he never so much as mentioned his experimental work on tumors, for he had long since passed to other problems. I did not even know at the time that he had done such excellent work in this field. The possibilities of the extension of the work were certainly not fully realized at that time. On the

whole, the investigation of tumors was almost exclusively limited to microscopic studies. Valuable and important as were the results given by these studies, there were noticeable the signs of exhaustion. The principal facts of the histogenesis and structural peculiarities of tumors arising from different types of tissues had been worked out as well as it could be done—in its main outlines, as well as in many of its details.

The similarity between metastatic and original tumor was established. There is now very little doubt that the epithelial tumors usually arise from a direct downgrowth of the epithelial cells, and that this downgrowth is sometimes at first entirely unaccompanied with changes in the underlying tissue. In carcinoma proper, the changes are primarily in the epithelial cells. The origin of cancer may be unicentric and start from one point, and this seems to apply to the majority of cases; or it may be multicentric, originating simultaneously from several points. The growth of cancer takes place through the multiplication of its own cells, usually without infecting other cells of the body. These are the main results of anatomical and histological studies; and they are, on the whole, well established. There are still a few points about which some doubt is justified. Especially debatable is, for instance, the origin of certain so-called mixed tumors. It is possible that some of these, instead of being of embryonic origin, are due to the influence exerted by one growing tissue upon another, the latter starting to grow secondarily.

So far, purely morphological investigations could go; but they were not able to give us any further information. They could not give us any insight into the conditions of the growth of cancer, and could not bring us any nearer to the understanding of its cause. Attempts to prove the presence of a distinct and specific microörganism in cancer by morphological or cultural methods have, so far, failed. No convincing evidence of their existence could be obtained; although I am by no means ready to say that, among the various structures found in cancer and described by many authors, there may not have been protozoa. The attempt to fill with hypotheses the gaps, where facts were missing has led to the constructing of many theories of the cause of cancer. Either these theories are enlargements upon one single fact, frequently in a purely specula-

tive manner; or they are based upon erroneous observations, as is the case with Ribbert's theory. There is no need to build up hypotheses prematurely, while we see before us a large field for work. First let us find as many new facts as possible and analyze these. There will be no difficulty in drawing our conclusions when we shall have sufficient data. These are what the more recent phase of the investigation of cancer promises to give us.

I refer to the experimental investigations of cancer in animals. That different animals may be afflicted with cancer has been long known, but our knowledge has been markedly increased within recent years. We are now able to make a certain number of generalizations, which are not without interest. In the first place, it has been established that not only parasitical pseudo tumors but that typical malignant tumors occur in cold-blooded animals.

Secondly, some species of animals are much more frequently afflicted with cancer than others; cattle, more frequently than sheep; dogs, more frequently than either of these; mice and rats, much more frequently than rabbits and guinea pigs.

On looking over the character of different tumors that are found in different animals, I find that in certain species certain distinct types of tumor are prevalent. Eight years ago, I found that by far the most frequent variety of malignant tumors among cattle in America is the squamous-cell carcinoma of the inner canthus of the eye. In dogs, the lymphosarcoma of the genital organs is very prevalent in America and Europe. In white rats, several sarcomata have been found by myself, as well as by Velich, von Eiselsberg, and Firket. Sarcoma seems, therefore, to be a relatively common tumor among white rats. This tumor appears, however, to be rare among white mice; but these animals are liable to another very common tumor, a subcutaneous carcinoma, or adenocarcinoma, which in many cases, at least, seems to take its origin from the mammary gland. This is by far the most frequent tumor in white mice. Among fishes, also, a certain type of tumor is characteristic for certain species; as the carcinoma of the thyroid in trout We occasionally find, of course, other tumors in these animals; but those just named are the most common.

Fourthly, a fact of great importance that has been observed in different animals is that tumors occur in them endemically. This

means that tumors are very frequent among them in certain localities. In Wyoming, I found, with Dr. Jobson, a ranch on which for ten years carcinoma of the eye has been endemic among the cattle, although the neighboring ranches are practically free from the disease. Among caged animals, the endemic occurrence of tumors has been found by Hanau, Morau, Borrel, Eberth and Spude, Michaelis, Gaylord and Clowes, and myself in the case of carcinoma; and by myself in the case of sarcoma.

Even among fishes, the endemic occurrence of cancer has been observed during the last few years, having been very carefully described by L. Pick. It is well known that an endemic occurrence of cancer has also been found in man; and especially Behla, Lyon, and Sticker have investigated the conditions prevailing at such places very carefully. There is, however, one very important difference between the endemic occurrence of carcinoma in man and in animals, to which I called attention three years ago; namely, that while in man different varieties of tumors were observed in the affected area, in animals it was always precisely the same kind of tumor that was observed—namely, squamous carcinoma of the canthus of the eye in cattle, sarcoma of the thyroid in white rats, squamous-cell carcinoma of the vulva in Hanau's rats, adenocarcinoma of the subcutaneous tissue in mice, and carcinoma of the thyroid in fishes.

This is one of the reasons why the endemic occurrence of tumors in animals is so much more favorable for investigation than is the endemic occurrence of cancer in man. Furthermore, in animals we can vary the conditions of life at will much more readily than in man, in whom the number of variable factors is so much greater. In animals, which can be kept in small cages over long periods, the conditions can easily be arranged, according to one's purpose. It is clear that an investigation into the cause of the endemic occurrence of cancer is of the utmost importance.

Three sets of conditions have to be taken into consideration: (1) Hereditary influence, which could cause cancer to appear in certain families of animals: (2) infectious conditions, the transmission of an organism from one animal to another, either directly or by means of a host; and (3) environmental conditions, conditions of the food, water, etc.

My former observations did not permit me to decide definitely

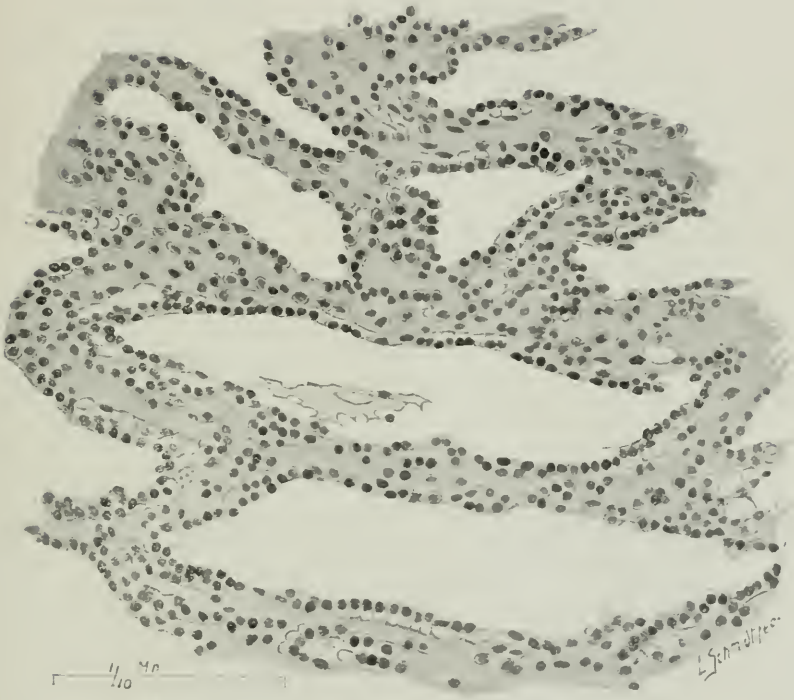
between hereditary and infectious causes. Some recent investigations of another case of the endemic occurrence of cancer in mice have suggested to me the existence of hereditary factors; but some known observations of others seem to point to an infectious cause. I refer especially to those of Haaland, from the Pasteur Institute, and to the recent communications of Gaylord and Clowes. The latter observed three cases of sarcoma in rats confined in cages in which, several years previously, some of my sarcomatous rats had been kept for about five months. The question cannot, as yet, be regarded as absolutely decided. It is quite possible that a combination of factors is responsible for the endemic occurrence, but there is very little doubt that the problem can be decided in an exact way. It is necessary only to have the requisite means and enough time. There is no doubt, also, that such an investigation is of the utmost importance. It brings us in direct contact with the cause, or with one of the causes, of cancer. Here we see tumors newformed in animals, without inoculation from another tumor. Ordinary tissue-cells, such as the cells of the thyroid of a rat, are transformed, as in my case, into sarcoma-cells, a long time after the animals previously affected with the tumor have been removed from the cage.

The same cannot be said of the second set of investigations to which I should like to call your attention. I mean the production of a tumor in an animal through inoculation with material from another tumor of the same species. In this case we do not convert previously normal cells into tumor-cells, but we make tumor-cells grow in other animals. The metastases of a tumor in the same animal can in this way be regarded as an autotransplantation of tumor-cells. In a similar way as a cell or a multicellular organism can be produced only if there has been previously present another cell, so a tumor can under these conditions be formed only if there has been another tumor present at the start. Notwithstanding this fact, the experimental production of tumors through the inoculation of tumor-material is of the greatest importance, inasmuch as it is likely to give us an insight into the conditions of the growth of tumors that could not be obtained in an exact manner in any other way; and secondly, because it permits us to investigate the conditions under which an immunity against the growth of tumors can be produced in animals.

Now it might be argued that while transplantation into other animals can teach us the conditions under which cells grow after they have once been converted into tumor-cells, and can show us the existence of immunity or predisposition to the growth of such tumor-cells; it can show us nothing about how normal cells become converted into tumor-cells. I myself distinguished sharply between these two sets of factors in my earliest investigations on tumor experimentation. Some experiences, however, suggest that there may exist a relation between the inoculability of a tumor and some of the conditions that favor the primary development of such a growth. In experiments on an adenoma of the mammary gland in a white rat, carried out in 1901, I found that the behavior of pieces of tumor when transplanted into the animal affected with the primary tumor, was very different from their behavior when transplanted into other rats. The tumors grew or remained alive in the former; they died in the latter. Similar results were obtained in experiments that I carried out last winter with Dr. S. Leopold on a mammary tumor of a dog. In the course of repeated inoculations, it was shown that pieces of tumor transplanted into the bearer of the primary carcinoma remained alive, but that they died, when transplanted into other dogs. In a similar way, in the course of inoculations of tumors into white mice, one experiment showed distinctly that a mouse affected with a spontaneous tumor, similar to the one inoculated, evinced a predisposition to the growth of the inoculated tumor. The conditions that made this animal a favorable soil for the growth of the primary tumor favored the growth of cells that had already been converted into cancer-cells. This is an important point that should be tested in future experiments; and it leads to a further question: Can all tumors be equally well inoculated into other animals?

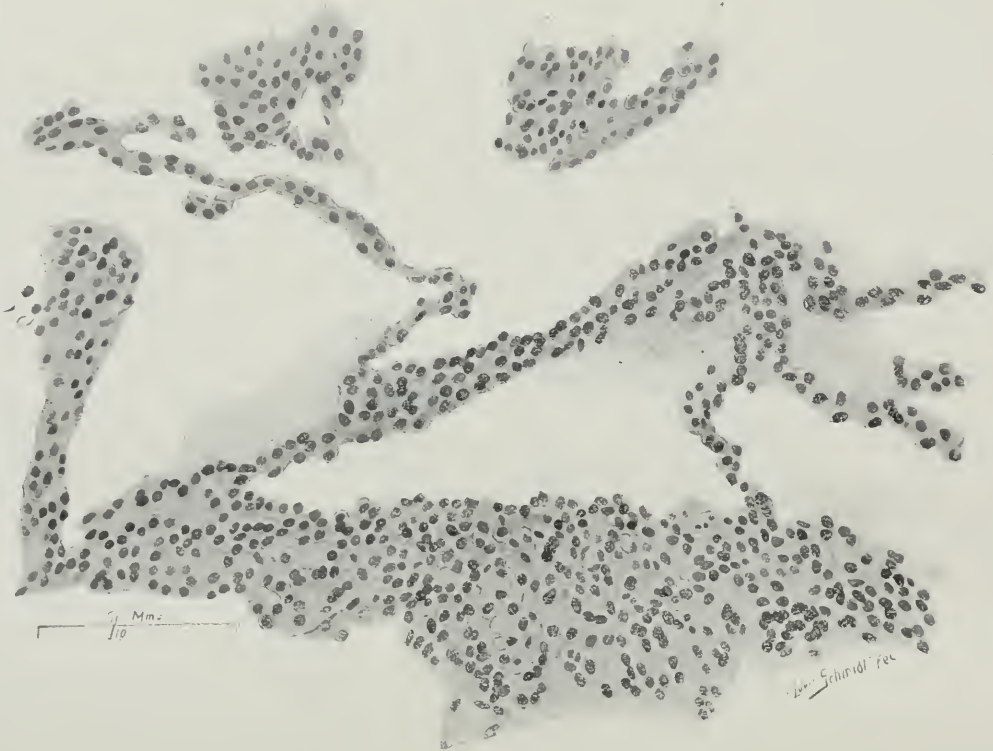
No, there exist differences. Certain tumors are much more likely to grow in other animals than are other tumors. Carcinoma, as well as sarcomata, have been successfully transplanted; and other sarcomata or carcinoma could not be transplanted. On the whole, however, it seems probable that my prediction that sarcomata will be found more readily amenable to transplantation will be borne out by the facts; at least, our experience so far tends to prove this. A certain percentage of tumors have been transplanted success-

Fig. 1.



Cystic sarcoma of the thyroid of a white rat. Original tumor.

Fig. 2.

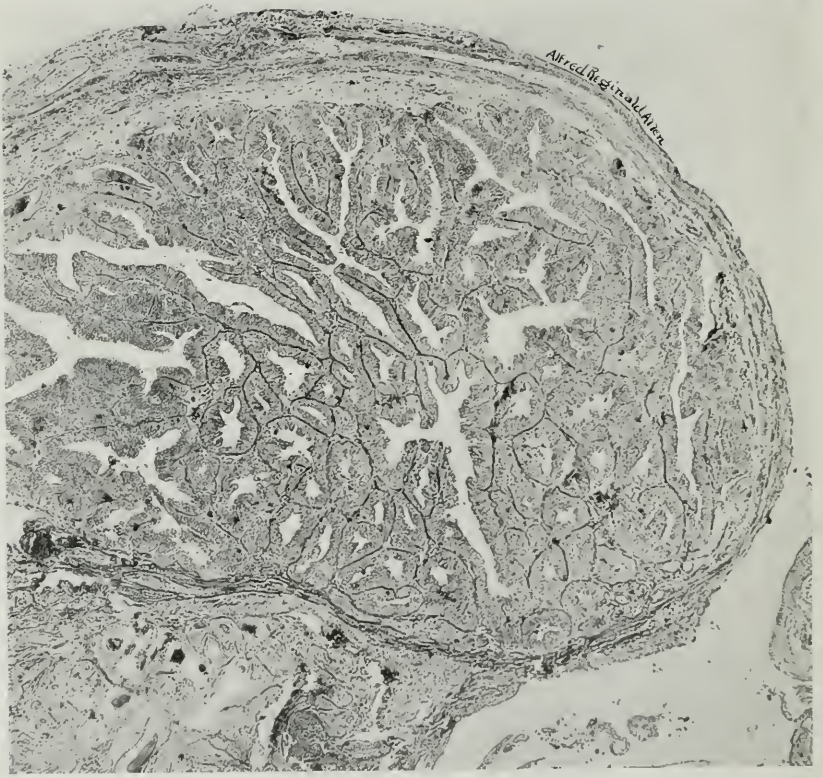



Cystic sarcoma of the white rat. Transplanted tumor.

Fig. 3.

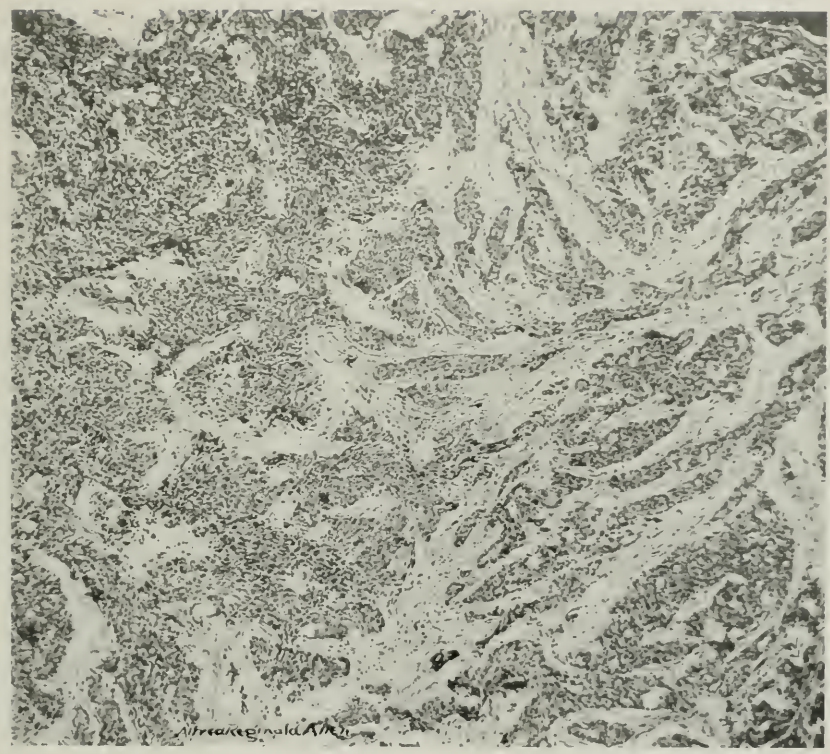
Cystic sarcoma of the thyroid of a white rat.

FIG. 4.



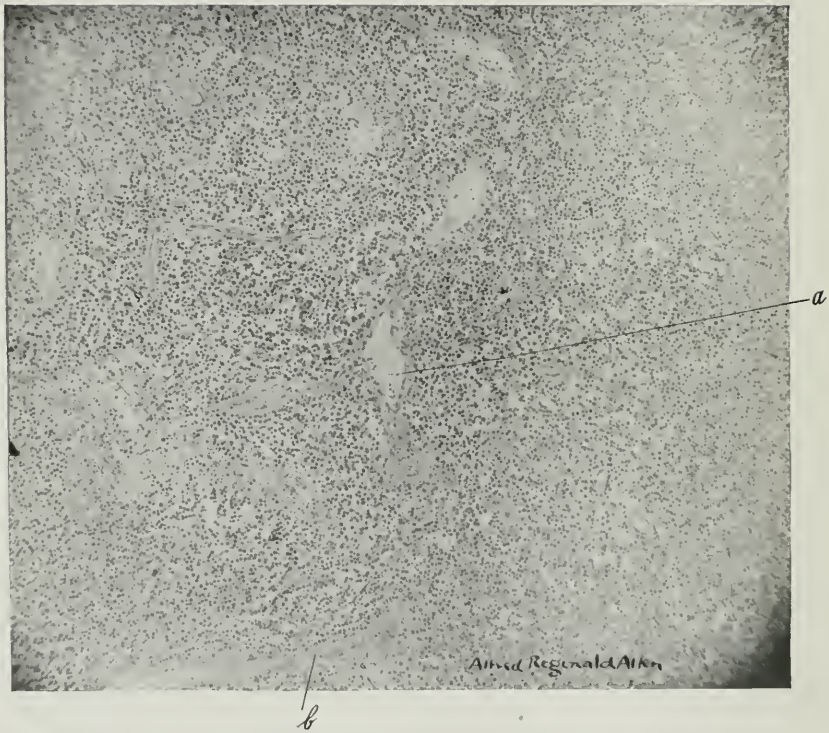

Papillary adenocarcinoma of a white mouse. This was not found to be transplantable.

FIG. 5.



Adenocarcinoma of a white mouse. In all probability originating from the mammary gland.

FIG. 6.




Lymphosarcoma of dog. This tumor was found in the wall of the vagina of a dog; it was readily transplantable. *a*, blood-vessel; *b*, stroma.

fully. In the course of sarcoma of the thyroid in the rat, the readiness with which the tumors of the four rats afflicted with primary sarcoma of the thyroid could be transplanted decreased gradually. The sarcoma of the first rat could be transplanted most readily. The last, sarcoma, with which I am now experimenting, gave the smallest number of successes. The others had an intermediate character. This is a remarkable fact which should lead to further investigation. In mice, a large number of subcutaneous adenocarcinomata cannot be transplanted. Others of a similar structure can be readily transplanted, and yield a large number of successful inoculations; while still others give only a very small number of successes. In dogs, the lymphosarcoma found in the genital organs is usually very readily transplanted; although other tumors of the dog show themselves refractory, in most cases, to successful inoculation. The three tumors mentioned are just the ones that have principally been used for inoculation, and I am in a position to-night to show you living animals affected with these three varieties of tumor. Ehrlich has also recently succeeded in a large percentage of cases in transplanting a chondroma found in a mouse.

If we now inquire into the causes of the difference existing in the inoculability of different tumors, we can mention a number of conditions that are of importance in that respect; but some work still remains to be performed. As I have already stated, I have investigated the differences in the inoculability of the primary cancerous animal and other animals carrying a similar primary tumor, on the one hand, and of other animals of the same species, on the other hand. I found that males and females, young and old animals, can approximately be inoculated to an equal degree; but I also found that certain animals cannot be inoculated, even when repeated attempts are made. Similar observations have been reported by Herzog, Jensen, and Ehrlich. Certain animals are refractory to inoculation with certain tumors. Michaelis, for instance, has made the interesting observation that certain strains of white mice may be more readily inoculated with carcinoma than others. There exists, therefore, a natural immunity in certain individuals against inoculation with tumor-tissue.

I have recently given especial attention to the question whether

pregnancy favors inoculation, but I have been unable to find any distinct influence. We see, therefore, that, in the first place, the predisposition or immunity of the animal is of importance; but secondly, the character of the tumor itself has to be considered. Different tumors behave very differently in this respect, even when they have the same structure. I have mentioned the difference of this nature existing in the four sarcomata of the thyroid, which had an almost identical structure. Their inoculability was very different. The same holds good in the case of the carcinoma of mice. Many carcinomata in white mice are practically untransplantable. Three years ago, I transplanted a carcinoma in a Japanese mouse. Its structure did not materially differ from that of the carcinoma of the ordinary white mouse. I was able to transplant this tumor successfully in 100 per cent. of the cases. The lymphosarcoma in dogs can also be transplanted in almost 100 per cent. of the cases; while other tumors of the dog cannot be transplanted at all, or only with difficulty. Perhaps we might be more successful if, for inoculation purposes, we could obtain the same variety of dog as the one in which the original tumor is found.

If we now analyze still further the second set of factors, namely, those dependent upon the peculiarities of the tumor itself, we find that the energy of growth in the primary tumor is not the only factor that determines the inoculability of the tumor; although it is one of the factors to be considered. In the case of the carcinoma of the Japanese mouse, I found that in the original animal and in the first generation of transplanted animals it grew very slowly; nevertheless, it proved to be inoculable in 100 per cent. of the cases. I have recently observed that multiplicity of tumors does not necessarily favor inoculability. I was able to make this observation after having obtained simultaneously from one breeder three mice with multiple carcinoma. One of these animals had as many as nine tumors in different parts of the subcutaneous tissue or near by. We see, therefore, that the inoculability of tumors depends upon a large number of conditions, which offer a fertile field for further investigation.

In this connection I may be permitted to draw attention to certain experiences, which are, perhaps, not without practical interest. I found in the case of my sarcoma in rats that the number of

Fig. 7.

Mouse with multiple carcinomata.

contact-metastases in the animal operated upon, depends upon the readiness with which the tumor can be inoculated into other animals. The first tumor, which could easily be transplanted, made the largest number of contact-metastases. Approximately at the same rate as the inoculability decreased, the contact-metastases decreased *pari passu*. The important point is this: we cannot determine beforehand from the structure of a tumor whether or not it is likely to make contact metastases. The tumors may have a similar structure, yet behave very differently in this regard.

Now let us consider the second phase of the experiment: A tumor has been found to be transplantable; and the next question is: How does it behave during transplantation into further generations? Does the inoculability gradually decrease and does it end after a certain time? This does not need to be the case. My first sarcoma I transplanted into forty generations, and only accidental conditions prevented its further inoculation. Jensen's carcinoma has continually been undergoing propagation in several laboratories for the last five or six years, and there is no sign of diminishing inoculability as yet. I found in my first experiments that the transplantation of a very few cells, in mitotic division, present in the cystic fluid of the sarcoma, suffices to produce the largest tumors. This suggested to me, six years ago, the conclusion that ordinary somatic cells (ordinary connective tissue cells or epithelial cells) have a much greater propogating power and the possibility of a much longer duration of life than had hitherto been supposed. It appeared to me possible that they might be immortal in the same sense as the germ cells are believed to be immortal. The experiences in tumor inoculation certainly suggest new lines of biological research that will be of great general interest. However, not all tumors can apparently be transplanted indefinitely, even if no accidental infection takes place. Morau noticed a gradual decrease in virulence in his tumors; although, even in this case, we cannot exclude with certainty the idea that accidental weakening influences, such as certain bacteria, had not been gradually inoculated simultaneously with the tumors.

In regard to the energy of tumor growth, some interesting conditions have been discovered to exist. As I pointed out two years ago, it is of frequent occurrence that the original tumor grows

more slowly than the transplanted tumors. The maximum rate of growth may be reached in the second generation. This was especially marked in the course of my transplantations of the adenocarcinoma of the Japanese mouse, but I had noticed it in my early transplantations of a sarcoma. Other observers have made some similar observations.

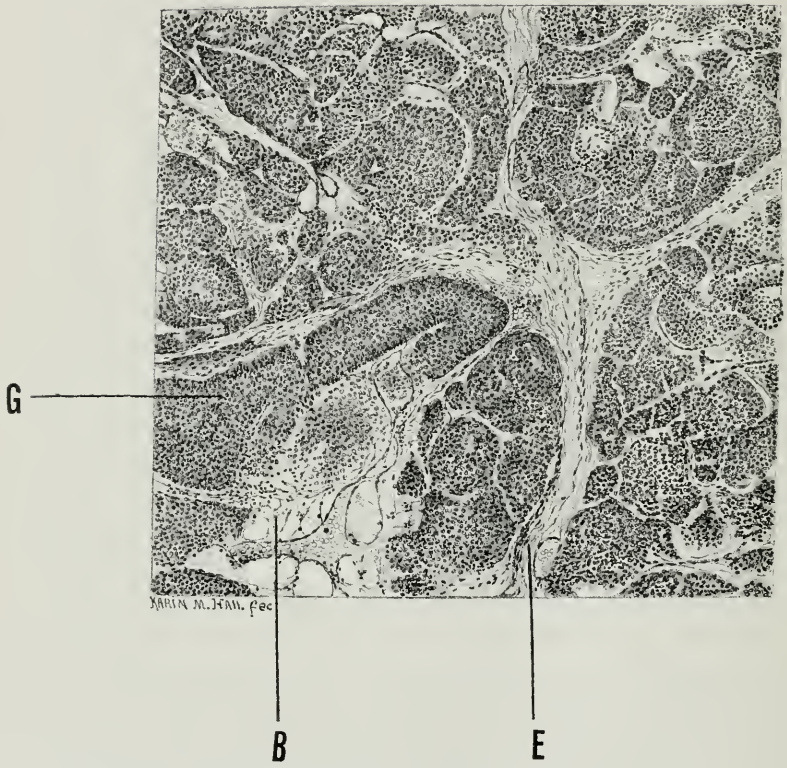
As to the cause of this increase in the energy of tumor-growth, I think it depends mainly upon the operative interference with the tumor, through which it is possible to stimulate its growth. It is possible to obtain a similar stimulation of growth through cutting a piece of tumor or pulling a silk thread through the tissue. In this way, I succeeded in causing tumors that had ceased to grow to start a fresh and vigorous growth. This experiment does not, however, succeed with all kinds of tumors. An adenocarcinoma of the breast of a dog, with which I experimented last winter with Dr. S. Leopold, proved refractory in this respect. The effect of injury upon the tumor does not depend upon the production of a better blood supply; for on microscopical examination this was not found to exist in my specimens. It evidently depends upon a directly stimulating effect of the experimental conditions upon the energy of growth of the cells, and it explains the observations of surgeons that recurrent tumors may grow more rapidly than the original tumors.

It is also possible to diminish the virulence of tumor-cells directly, by subjecting them to certain physical or chemical conditions, *e.g.,* by heating the tumor-cells up to 43° or 44° for half an hour outside the body. Certain chemicals act in a similar way. This decrease in the energy of tumor-growth is caused by a directly depressing effect upon the tumor-cells, or upon the agency included among them that causes the growth. The important bearing of this fact upon some practical problems will soon be discussed. The knowledge that it is possible to decrease the energy of tumor growth experimentally, without killing the cells, came to me quite unexpectedly. The experiments of Sticker, Ehrlich, Apolant, and Michaelis have confirmed my own results. If we increase the strength of the injurious influence but slightly, the tumor-cells are killed. The destructive effect of certain external agencies was determined by me for sarcoma; and independently of me, at about the

FIG. 8.

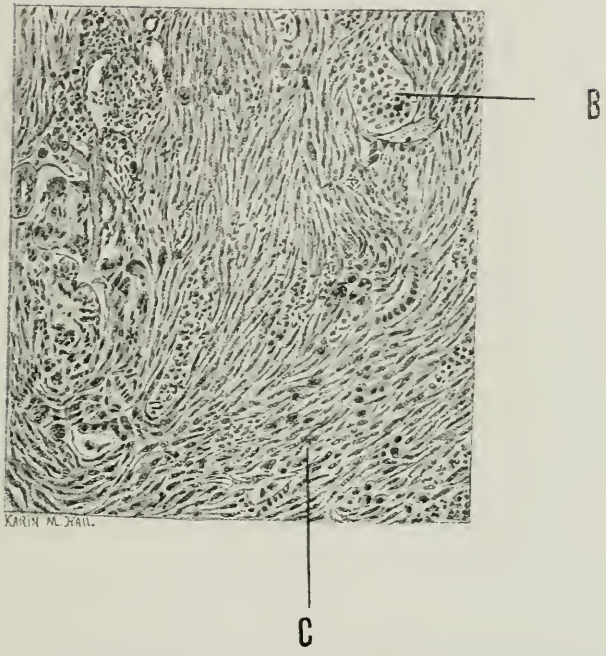
Original carcinoma in Japanese mouse. *i, a, b, c, e, g,* ramification of ducts. In the inoculated mice carcinomatous and sarcomatous tumors developed.

Fig. 9.




Carcinoma of the Japanese mouse. II inoculated generation. G, carcinomatous cell masses. B, E, stroma.

Fig. 10.




In the II generation inoculated with the carcinoma of a Japanese mouse, spindle cell sarcomata are found besides the carcinomatous tumors.

same time, by Jensen for carcinoma. It is interesting that there is scarcely any difference in this respect between sarcoma and carcinoma. There may, however, be a minor difference of about 2° or 3° in regard to the action of heat on different tumors.

Clowes and Baeslack have recently found that, if the temperature to which the tumor is exposed outside the body before inoculation be still lower, and only slightly higher than the body-temperature, the energy of tumor-growth is increased. It is probable that this stimulus is of a similar kind to the one observed by me in threading a tumor or excising a part of it. Another method of increasing the energy of tumor growth has been used in recent years by Ehrlich. He uses in such series of inoculations the most actively-growing tumor, and believes that in this way he has, by selection, obtained a race of tumors with increased virulence.

A question of great interest is, whether inoculated tumors preserve their morphological characteristics during the course of their many generations of life in other organisms. In general, they do. Sarcomata, as well as carcinomata, occasionally, however, exhibit slight transitory variations as described by me in my first paper on transplantations of tumors. A sarcoma may assume a somewhat endotheliomatous structure, and the type of growth of an adenocarcinoma in mice may undergo slight changes; but, on the whole, the structure remains preserved. Only one very marked exception has been noted; namely, the appearance of a spindle-cell sarcoma in the course of the transplantation of a carcinoma, which I observed three years ago in a Japanese mouse, and which Ehrlich and Apolant noticed approximately at the same time. In my case, the sarcoma originated as early as the first inoculated generation; in Ehrlich's, it was found only in later generations. A fact of general interest is that in my transplantations, the curve indicating the variations in the energy of growth in different generations applied equally to the sarcomatous and to the carcinomatous components. This suggests that the same factor underlies the growth of the sarcoma and that of the carcinoma. In both cases, the carcinoma and the sarcoma could be mixed or entirely separated in the different animals. Do we have to deal with a transformation of carcinoma into sarcoma? Although there are places that might be interpreted as indicating such a transition, a careful study of the differ-

ent tumors in very many sections makes it more likely that we have to deal with a conversion of connective-tissue cells into a sarcomatous growth. The epithelium transmits its stimulus to grow to the connective tissue of either the original animal or of the host. As I have mentioned above, these observations may throw some light upon the origin of such tumors as the sarcoma-carcinoma of the thyroid. Instead of assuming that they are due to congenital malformation, we may, with as much justification, hold that primarily one tumor (a carcinoma) was present, and that only secondarily a stimulus emanating from the carcinoma caused the connective tissue to assume a sarcomatous growth.

We now turn to a question that is of theoretical, and promises to be of practical importance, namely, that of immunity. In the foregoing I have already mentioned some facts that have a bearing upon this problem. We see that certain animals of a species are immune, while others are predisposed to the growth of an inoculated tumor. I have not infrequently observed, in the course of my tumor-inoculations, that certain tumors, after a preliminary growth, become stationary, or may even retrogress. Mitoses may be present in these latent nodules for a long time, until mitotic divisions entirely cease to take place.

Animals with merely stationary tumors may still constitute a favorable soil for tumor-growth, as I found during my inoculations of sarcoma. Sticker, however, found, in the lymphosarcoma of dogs, that as soon as an animal has entirely recovered spontaneously from an inoculated tumor, it has become immune against any further tumor-inoculation. Clowes and Baeslack observed the same fact in the case of carcinoma in white mice. They found, moreover, that the serum of such spontaneously-recovered white mice has a certain, althought only a very slight, immunizing effect against tumor-inoculation upon other mice. Sticker likewise observed a certain curative effect of such serum upon other dogs affected with lymphosarcoma. These observations are probably to be explained in the following way: In a certain number of animals that seem to be predisposed to acquire an active immunity, the latter is acquired as the result of the temporary growth of a tumor. This immunity is an active one, and the serum acquires certain cytocidal properties in vivo. This serum has, however,

no agglutinating properties upon a tumor-emulsion; certain antibodies are, therefore, lacking, as Sticker found.

But not all animals in which a tumor has been growing for some time have thereby become immune. Such animals may, as I very early observed in my experiments, be successfully inoculated with another tumor. Here I am able to show you a dog inoculated several months ago with lymphosarcoma, and reinoculated about four weeks ago. The second tumor is growing. Ehrlich has, however, recently found that when a mouse is inoculated with a very rapidly-growing carcinoma, a second inoculation with a carcinoma will not be successful. In this case, the animal has become immune through the first inoculation.

The next step was to find a method by which to immunize animals actively against the tumor-growth. This applies as well to preventive immunity as to curative immunity. The principle that may have to be applied for this purpose is the one announced by me more than three years ago, in a paper before this Society; namely, the use of a virus of decreased virulence. I found especially effective for the production of such a vaccine a graded exposure to higher temperatures. Exactly the same method has been successfully applied by Michaelis [1] in the Berlin Institute für Krebsforschung within the last year. At first he used tumor tissue killed by chloroform for his experiments, but entirely without success. Neither was he able to obtain an active immunity by inoculating the tumors of gray mice into white mice, or vice versa. Ehrlich, however, obtained an active immunity by using for inoculation tumor-material that was originally less virulent; for instance, hæmorrhagic carcinomata in mice.

Of theoretical interest is the fact that an active immunity against certain tumors of mice can be produced by injecting mice with different varieties of tissues of the mouse; for instance, embryonic tissue and sarcomatous tissue. Conversely the injection of carcinomatous tissue protects against sarcoma. Evidently we have here to deal with an active cytolytic property of the body acquired through the injection of cells of the same species. Practically, however, the inoculation of living tumor-tissue of ordinary viru-

[1] We have to suspend our definite judgment in regard to his results, until his more detailed report has been published.

lence cannot be carried out in man; and von Dungern's experiments in the production of an active cytolytic immunity by injecting human milk into man seems to have failed. Probably we shall again have to consider the use of a vaccine prepared by experimentally decreasing the virulence of tumor-material. Very interesting results have been obtained by Sticker, who found in the lymphosarcoma of a dog, that a single intravenous injection of a suspension of tumor-material produces an active immunity in dogs, without ever leading to the new formation of tumors. We see that we shall have to study the conditions under which an active immunity can be produced in different animals, before we can contemplate the use of such means in the case of human tumors; especially as it is quite probable that different varieties of tumors in animals and man behave somewhat differently in that respect.

As to a passive immunity, which means the use of the serum of actively immune animals for the cure of tumors, I can be brief. Since the first experiments of Richet and Héricourt, twelve years ago, many attempts have been made to cure tumors in man by use of a serum. Especially v. Leyden and Blumenthal are making and have been making for the last six years, systematic investigations in this direction, without, however, having produced very marked results. It is said that metastases do not develop under the influence of such serum. In mice, Jensen has used the same principle; but his results have not been of such a character that he could be convinced of the efficacy of the treatment. Other investigators have also tried it, without having reported any definite results so far. Perhaps the future will give better results. It seems to me, however, that active immunity will be the method promising more success than the use of serum.

Time does not permit me to discuss certain recent investigations into the chemical character of malignant tumors. Definite statements in that regard can scarcely be made, as yet; inasmuch as the cases examined have not been sufficiently numerous to justify definite conclusions. Certain differences seem, however, to exist between the chemical composition of tumors and that of the normal tissues from which they are derived. These differences are especially indicated by certain products found in tumor-tissues undergoing autolysis.

There is, however, one other phase upon which I should like to touch briefly; and that is the difference between the behavior of normal tissue and that of tumor tissue during the process of growth. Normal tissue, when transplanted, if it grows at all, does so for only a limited period; and then the growth ceases. There seems to exist a certain cycle in the response of a normal tissue to a stimulus. I thought it possible that the action of the surrounding host-tissue prevents the further expansive growth of the transplanted epithelium. Therefore, in the course of the last three years, I have carried out a large and varied number of experiments in which, at different stages of its growth, I liberated regenerating tissue from the influence of the surrounding connective tissue by re-transplanting it into other animals. This was repeated a number of times in succession. The result was identical in all the experiments; regenerating epithelium always retained its general properties. It remained regenerating tissue, and did not assume the expansive or infiltrating growth of tumor-tissue. A summation of the stimuli that might lead up to tumor-growth, did not take place.

We may, therefore, conclude that, under the influence of localized stimuli, of whatever character they may be, a malignant growth of cells cannot be initiated. Such cells, under the influence of localized stimuli, grow as long as the stimulus exists; and then they return to their former state of equilibrium. Transplanted into another animal, in which the same stimulus would no longer be present, they behave like ordinary regenerating epithelium. We are forced to conclude, from all the experiments that have so far been carried out on normal tissues, that an hereditary transmission of the changes produced by such stimuli upon certain cells cannot take place. Whether or not such an hereditary transmission does exist, was one of the questions that I have tried to answer by the experiments in the successive transplantation of tissues. As we have seen, there is no indication that such an hereditary transmission can ever take place. Until this is proved we have to assume, in order to explain the growth of the malignant tumors, that can be inoculated into other animals, the constant presence of a certain stimulus in or around the tumor-cells themselves, a stimulus that remains connected with the tumor-cells into whatever animal these cells may be transplanted.

What I have just now said in regard to localized stimuli holds good of stimuli originating at points of the body farther distant. I may illustrate this with an observation that I have made in recent years. Towards the end of pregnancy, the atresia of follicles in the ovaries of young guinea-pigs can assume a specific character, distinguished by a marked hypertrophy of certain cells. Such changes may be multiple. We have a right to believe, in this case, that a stimulus not unlikely of a chemical character is produced outside the ovaries, leading to this hypertrophic change in the follicles of the ovary. Transplanted into other animals, however, such changes would not progress in the follicles; because the stimulus that had initiated them would no longer be at work.

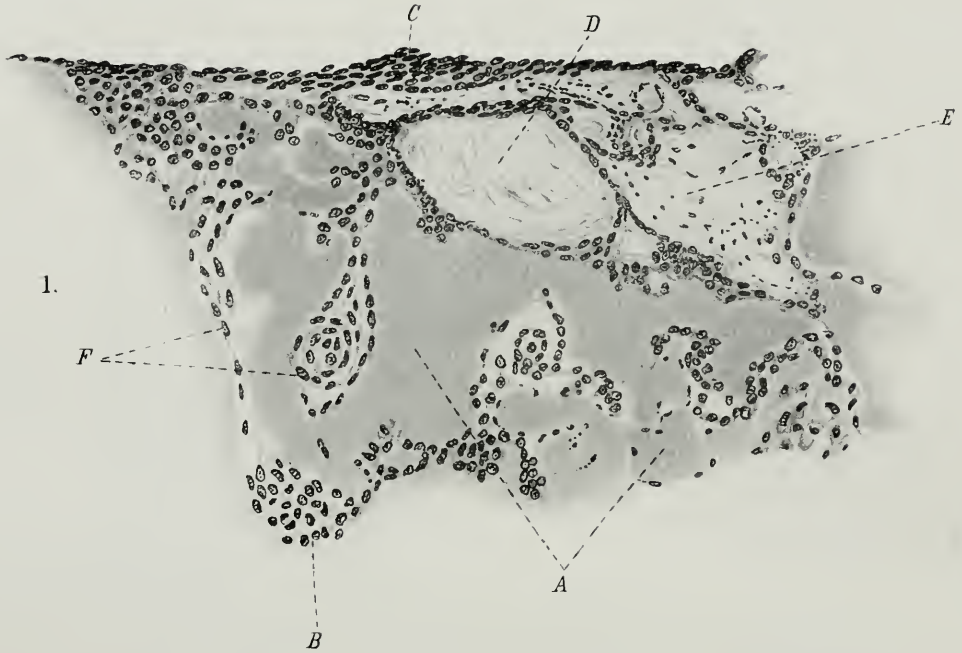
Localized stimuli, and those coming from more distant parts of the body, may lead to what might be called transitory tumors, tumor-like, new formations that show a definite cycle in their development. They grow up to a certain point, so long as a certain stimulus is present; then they gradually retrograde. The corpus leutum may be regarded as the prototype of a transitory tumor. The small syncytiomata in the ovaries of very young guinea-pigs, which I found to be present in about 10 per cent. of the animals, also belong to that class. They reach a certain development, and then retrogressive changes take place. In a wider sense teratomata may likewise be placed in this class if they remain dormant; as well as other tumors that would cease to exist if transplanted into other animals in which a stimulus calling forth their proliferation would no longer be present. The course of such typical malignant tumors that seem to grow indefinitely in other animals can, however, be explained only if we assume that the tumor-cells carry with them the stimulus that causes their proliferation.

In conclusion, I wish to say that I believe that the tumor problem must at first be regarded as one of biology, and must be dissociated from any considerations of practical medicine. We have to analyze this problem as a part of the problem of growth in general; although any insight into the application of the knowledge we may gain through purely theoretical studies will certainly, in the end, benefit medicine.

Fig. 11.

Epithelium growing into Agar. A number of branches are formed (D) (E), A, Agar. C, connective tissue. Regenerative growth is quite distinct from tumorous growth.

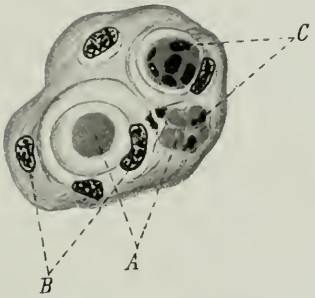
FIG. 12.




Growth of epithelium of a guinea pig in coagulated blood-serum. A, blood-serum. B,F, epithelium growing into the blood-serum. D, Keratin. E, connective tissue. The growth of the epithelium may take place without connective tissue. The growth ceases after some time. Carcinoma does not develop from transplanted cells.

Fig. 13.

5.




Epithelial pearl developing in epithelium in coagulated blood-serum.
See explanations of Fig. 12.

FIG. 14.

Skin of a guinea pig after a series of retransplantations. Large masses of horn are formed. In the periphery there is a layer of living epithelium and connective tissue. No tumor-like growth has taken place.

Fig. 15.

Small transitory tumor in the ovary of a young guinea pig. Such tumors are found in about ten per cent of all young guinea pigs and have frequently the character of a syncytioma.

# THE SURGERY OF THE BLOOD VESSELS

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At the very bottom of all true surgery lie two fundamental ideas; that the surgeon should do as little damage as possible to any except the diseased tissue, and that he should restore the tissues as nearly as possible to their normal position, not only to the normal position of the organ as a whole, but that each separate part of a complex organ shall be replaced in its normal position. This, it seems to me, must be the main advance of the surgery of the future, with its more delicate and finished technique. These two ideas must be borne in mind with a peculiar vividness in the consideration of the surgery of the blood vessels.

If we consider our subject from the historical standpoint, the oldest idea involving the surgery of the blood vessels is that of the transfusion of the blood from one human individual to another, or from an animal to a human being. In those early days commonly thought of as the breaking of the dawn of history,—and yet may they not have been the twilight of a still earlier day?—we find references concerning the transfusion of blood. According to La Martinière[1] it is to be seen in the history of the ancient Egyptians that these peoples practiced transfusion for the healing of their princes. A review of an ancient Jewish writing[2] which was shown to La Martinière by Ben-Israël Manassé, a rabbi of the Jews of Amsterdam, contains the following words: "Naam, prince of the army of Ben'Adad, king of Syria, being attacked with leprosy, resorted to physicians who, in order to cure him, withdrew blood from his veins and replaced it with other blood." At a much later day Libavius,[3] in his treatise upon the sacrifices of the Emperor Julian, speaks of transfusion, as having been an eye-witness of an operation of this sort. There are many other references to be found by the curious, and to be believed or disbelieved as one may choose, since we have no proof, which bring us down to the middle of the seventeenth century. The discovery, or re-discovery, of the

circulation of the blood by Harvey, in the early part of the century, coupled with the then prevailing philosophical, or mystic, conjectures concerning the real functions of the blood, made the question of transfusion one of unusual interest. The earliest experiments seem to have been made in England in 1657 by Clark, and about the year 1666 by Lower and Boyle.[4] In the year 1667, Denis,[5] professor of Philosophy and Mathematics at Paris, performed the first transfusion operation upon a human being—that is, the first operation the account of which we find preserved in an original record. In the fall of the same year Lower and King operated in London.

It would be a matter of much interest to follow the history of the operation, but it would also be a tremendous undertaking. Gesellius[3] has collected toward one hundred references from the older literature, *i.e.,* up to 1803, and one hundred and sixty-nine references from that date to the year 1872. The two following decades would doubtless show a still larger number of papers bearing upon the subject. Landois [6] in 1875 collected three hundred and forty-seven cases of transfusion of human blood, of which in one hundred and fifty cases the result was favorable, in one hundred and eighty unfavorable, doubtful in twelve, while in three no result was to be expected, and two died during the course of the operation. He has also collected one hundred and twenty-nine cases of transfusion of animal blood into the human being, of which forty-two resulted in a cure or continued improvement; in twenty-five cases transitory improvement and doubtful success were noted, and sixty-two operations were followed by no improvement and death. These statistics are doubtless of little value, for all the operations were done before the days of asepsis, of bacteriology, and of modern knowledge of the finer processes of the coagulation of the blood and of thrombosis. For this reason one might say that they proved nothing; they do serve, however, to show the great interest which the operation has always excited in the human mind.

It would be of further interest, though of no practical import, to follow the discussions which the idea of transfusion occasioned from the days when men wondered if the transfusion of the blood of a lamb into a human being would give him a lamb-like character, or even cause him to grow wool and horns, to the days of the

question whether the blood should be defibrinated before transfusion. It is well worth the moment to consider that out of all this work and discussion grew directly the work of the past decade upon immunity, work which has given us such practical results as the medico-legal determination of blood by the biological test, and the determination of a state of infection by the method of complement deviation. In short, the fact of practical encouragement to any man of science, that the result of real endeavor is never lost.

A glance at this recent literature shows us one fact of emphatic importance. The blood of each and every species in the animal kingdom is peculiar; the blood of two species cannot be mixed, because agglutination and dissolution of the corpuscles always result. The corpuscles of the sheep, the blood of which animal has been most frequently used in the transfusion of animal blood into the human being, are dissolved by human serum in from three to six minutes. Human corpuscles are immediately agglutinated by the serum of sheep's blood and begin to dissolve after seven hours (Landois, lc. p. 156). Transfusion from one species to another would be an unpardonable error.

The invention of a method by means of which the artery of one individual can be made practically continuous with the vein of another individual, so that intima lies against intima and not even the finest needle holes pierce the vessel wall, excludes the possibility of coagulation, at least during the time necessary for a transfusion, and renders it futile to discuss the danger of embolism. This method consists in passing the cut end of the artery through a suitable tube, and turning it wrong-side out, back over the outside of the tube; this cuff, with the intima on the outside, is fastened in place by a ligature. The vein is then drawn over this cuff, and is fastened in its place by a second ligature. The ligatures are prevented from slipping off the little tube by placing them over grooves cut in the tube itself, or behind raised threads upon the exterior of the tube. This idea seems to have originated with von Quirolo.[7] A few years later, and apparently independently, Payr[8] adopted the idea in his method of performing the end-to-end anastomosis of blood vessels. Crile has made the idea extremely practical for the transfusion operation by attaching a handle to the little tube.

Given, therefore, a method which seems perfect, when shall we apply it? Obviously the general conclusion would seem at first thought to be that transfusion is indicated in all cases where there is a deficiency of blood, either an actual deficiency or a functional deficiency.

The active interest in the operation of transfusion was brought to an end, possibly only a temporary one, nearly thirty years ago by the work begun by Kronecker [9] upon the anæmia produced by acute hæmorrhage. This work shows that death from loss of blood occurs at a time when there are still a sufficient number of red corpuscles within the body to carry on the function of oxygenation of the tissues, but when the fluid volume of the blood within the circulatory system has been so diminished that the heart, so to speak, has lost its grip upon the blood column. If the fluid volume be now increased by a simple saline infusion, the heart can go on with its function and the patient will recover. The procedure called auto-transfusion, from the simplest method of lowering the patient's head, to that of bandaging the limbs, or the application of the pneumatic suit, acts in the same way, though to a less marked extent.

These facts seemed so conclusive that we can find in some of the most modern text books of Surgery statements such as this, concerning the operation of transfusion: ". . . Senn insists that the operation has proved an absolute failure. It does not prevent death from hæmorrhage, and the transfused blood-elements do not retain their vitality. . . . In fact, the operation of transfusion has become all but extinct. It exposes the patient to the danger of embolism and infection, its employment requires material and instruments often difficult to obtain in an emergency, and it has no single element of value beyond that secured by the use of salt solution, except in cases overcome by illuminating gas, in which a more prolonged good effect is produced than by salt solution."[10]

With a method at hand so ideal and so simple as that I have just described, the patient is not exposed to the danger of embolism and infection, and for this reason we find now a reawakening of interest in the operation of transfusion. The instruments are so simple that any one could have them,—the only difficulty is to find some one who is willing to sacrifice his radial artery. But even if

these difficulties, which might confront an emergency case, did exist, and granting that as much good can be accomplished in acute hæmorrhage by intravenous infusion of salt solution as by a transfusion of blood, there still remains a large group of cases to be considered where the instrumentarium can be prepared and where one has ample time to find the necessary radial artery. I refer to cases of functional deficiency, either of the blood itself, or of the organs which produce the various components of the blood.

In the case of an impairment of function of the red cell, the best example being that of poisoning with illuminating gas, where the blood producing organs are normal,—an emergency case, it is true,—transfusion would seem to be clearly indicated. But in those cases where the fault lies in some disturbance of the production of the constituent parts of the blood,—what then? The factors to be considered are too numerous to permit an answer without long and prayerful consideration.

The blood contains red and white cells and blood platelets; fibrinogen, salts, and water; agglutinins, precipitins, and various amboceptors and complements,—not to mention many other words of Latin and Greek derivation; further, the blood serum contains at various times and in varying amounts all the food stuffs for the somatic cells and all the products of their break-down. Beside the precipitins, the agglutinins, and the hemolysins always present in the blood of a given species, which are active against the bloods of every other species, there are indubitable evidences of the existence of iso-bodies, bodies of the same nature as the hetero-hemolysins, etc., which react with the blood of other individuals of the same species. In every transfusion the possibilities are to be multiplied by two, since each serum may furnish the active factors, each set of corpuscles the passive elements. Precipitation of the albuminoids, and particularly agglutination of the red or white cells, would cause capillary thrombosis. The setting free of the hemoglobin by hemolysis in the circulating blood is "the most powerful means of causing an instantaneous destruction of the leucocytes, and a sudden and extensive accumulation of fibrin ferment."[11] The expression of this ferment intoxication, according to its severity, would be fever, dyspnœa, hemoglobinuria, and sudden death due to extensive coagulation within the vessels.

Even before we consider these intricate biological phenomena there are many simple physical and simple chemical questions which occur to the mind of one who is at all familiar with the study of the blood. Such differences ought to be of small moment in the consideration of the action of one normal blood upon another normal blood, yet they might become paramount as soon as we enter the door of pathology. This is the reason why experiments on normal animals cannot answer the questions which arise in cases of pernicious anemia, or of hemophilia, etc. Among these simpler points to bear in mind is the fact that a transfusion suddenly introduces a large amount of available nitrogen into the blood. Now it is recognized by physiological chemists that a sudden increase of available nitrogen often precipitates an intensity of nitrogen metabolism which carries the nitrogen output far beyond figures which can be covered by the sum of the nitrogen intake of the food plus the available nitrogen from the newly added, transfused serum,—in other words, tissue breakdown is caused.[12] This point would need especial consideration in the cases we now have in mind, where the nitrogen equilibrium has been sufficiently upset by long continued illness.

I have often encountered the statement to the effect that it is probable that the newly transfused blood elements do not long retain their vitality. I cannot find any reason for this statement, unless, as I surmise, it dates from the time of the transfusion of alien blood. The blood elements of any animal would undoubtedly be destroyed by the human serum in a short time, the time varying according to the species. But there seems to be no reason, unless iso-hemolysins or some physical or chemical changes entered into the play, why the elements of the transfused blood from one individual of the same species should not retain their vitality for as long a time as if they were still in the body of their author. In the normal animal, blood cells are constantly dying and as constantly being replaced, an equilibrium being maintained. After the transfusion of normal blood into a pathological body the new elements would live their natural life,—other things being equal,—but would not all, at any rate, be replaced by newly formed elements. I think, therefore, that careful study would show evidence of a quantitatively abnormal destruction of red cells, such as the excretion of

urobilin, after every transfusion, and especially in those cases in which the blood producing powers of the patient are impaired by immediate disease or by general weakness. It is possible that this consideration of increased katabolism of the red cells would alone form a contra-indication to the operation of transfusion.

From a complicated operation with simple results the operation of transfusion has grown to be an extremely simple one, with results of illimitable possibilities for evil, at least. The practical man will consider transfusion from one human body to another an operation which can be performed by any surgeon under any circumstances, even general anæsthesia should not be employed, since the general condition of both giver and recipient is the best evidence of the amount of blood transfused. He should further look upon the operation as a possible means of saving life when all other means have failed, as a procedure of last resort; in acute hæmorrhage, if salt infusions fail, or if their effect is too transitory; in cases of certain death unless a constant loss of blood, as, for instance, from the mouth, be stopped, transfusion should be tried with the hope that the normal fibrinogen might seal the oozing pores; in poisoning with illuminating gas, in fact, in all cases where the fault seems to lie in the condition of the blood. Transfusion cannot be considered a specific treatment and is undoubtedly absolutely contra-indicated in many of these cases; yet the contra-indications are dependent upon such subtle factors that one cannot specify them, for we know too little concerning these factors. We know too little,—and, indeed, it may happen that practice will give the lie to theoretical pessimists.

The transfusion of blood still appeals to the laity as an operation savoring of the miraculous; therefore let every surgeon bear in mind that he who contributes most to the amazement of the populace generally also contributes most to the amusement of his fellows in the profession.

It is a relief to turn to our second subject, in an historically ordered study of the surgery of the blood vessels, the treatment of aneurisms. While the operation is more difficult, the results, even in unfavorable cases, are relatively easy of comprehension. It seems to be well established that Antyllos, in the third century, described the ligation of the artery above and below the sac, followed

by the opening of the sac itself in order to remove the contents without extirpation of the walls of the tumor. Almost from that day until the present the literature upon the subject has been continuously growing, so that it would now be a matter of little more than passing interest to enumerate even the methods which have been proposed for treating aneurismal tumors.

I shall assume that every one is sufficiently familiar with the pathology and the diagnosis of aneurisms, and with the indications and contra-indications of the operation, to permit me to disregard these points entirely. I shall consider only those cases where a surgical procedure in its truest sense can be employed, where a radical operation can hope to restore *ad integrum.* In many of the inoperable cases the older suggestions are still to be borne in mind, for they are often the only methods which are applicable.

These older methods for the treatment of such aneurisms as are suitable for a radical treatment are now rendered obsolete by the introduction of a method which conforms to the two fundamental laws of surgery laid down at the beginning of this paper, the method known by the name of its inventor as the Matas operation.[13] The first rule, to do as little damage as possible to any other tissue or part, is obeyed by not dissecting out the sac, thus leaving intact the collateral branches which open from the sac itself or from its immediate neighborhood. Matas's latest suggestion also fulfils the second requirement, the restoration of the parts to their normal position and function.

The operation is, briefly, in its essential principles as follows: The sac is laid open by a longitudinal incision, and the contents cleaned out. A rubber tube corresponding in size to the calibre of the artery is placed in the bottom of the sac; the walls are then brought together over the rubber tube in such a way that a new channel is formed, continuous with the openings of the artery into the sac. The rubber tube is withdrawn before the last few sutures which have been laid in place are tied. The openings of collateral branches in the walls of the sac outside the area used for rebuilding the arterial channel are closed with sutures, a procedure which must sometimes immediately follow the incision of the sac, because of hæmorrhage from these collaterals. The sac is then obliterated by laying its walls in a series of tucks, and placing these layers down

upon the newly made channel, in order to strengthen it on the outside, the point of least tissue resistance.

I am aware that the reconstructive operation is not always feasible, and that Matas himself recommends it only in a certain class of aneurisms. I think, however, that it represents the highest development of the methods for operating upon aneurisms, and stands as the goal toward which surgery should strive in all cases.

This description of so excellent a method is necessarily meagre because this is not the place to describe at length those methods which are to be found in a modern text book. I describe it thus briefly in order to show how this branch of blood vessel surgery has been made to satisfy the two fundamental laws of surgery. A possibility in the treatment of aneurisms is the transplantation of a segment of a normal artery or vein, a matter I will discuss later under the heading of the transplantation of organs.

Next in historical order is the problem of the surgery of the blood vessels, a question bearing upon the treatment of accident cases, and of cases where the extension of a tumor has involved the blood-vessel wall. Longitudinal wounds of blood vessels, and transverse wounds involving only a portion of their circumference are easily repaired; if such wounds are of slight extent in a vein, the lateral ligature is successful; if of greater extent in a vein, or if in an artery, they are simply sewed up. The question possessing the dignity of a problem is that of the repair of wounds which completely divide a vessel, the question of the end-to-end anastomosis of blood vessels.

The history of the surgical repair of blood vessels begins in the year 1759, when Hallowel, an English surgeon, at the suggestion of his fellow, Lambert,[14] attempted to repair a wound of the brachial artery, and perhaps succeeded. The literature upon the subject is not, however, relatively large, for the difficulties to be overcome were too great for the pre-aseptic age of surgery.

The consideration from the mechanical standpoint of the possibilities of uniting a tubular structure, whether it be a severed blood vessel or two pieces of pipe, leads to the conclusion that such hollow structures may be reunited in one of four ways; first, the ends may be brought as nearly as possible into exact juxtaposition,—in the case of blood vessels, approximating the various coats of the

vessel to each other; secondly, the edges may be everted, turning the edges outward in the form of flanges; thirdly, one end may be inserted into the other end, invagination; fourthly, a mechanical aid may be employed,—some form of the "union" of the plumber. The method of exact approximation has given the best results in experimental work.[15] The method of invagination has been most often used in human surgery.[16] The use of a "union" appeals to some minds as being the most rational.[8] It is probable that the question will ultimately prove to be not so much one of method as of technique.

The results of experimental work incline me to the belief that the method of exact end-to-end approximation is easier of execution and, since it fulfils the fundamental law, the restoration of each part of a compound organ to its original position and function, is perhaps theoretically correct.

There seems to be unity of opinion in the descriptions of the various methods which have been tried as to the choice of suture material. This should be a fine silk, of a size carefully chosen so as to fill completely the hole left by the needle. The needles should be of the smallest possible size, round pointed, and either straight or curved according to the individual and the site of operation. Experimenters are further agreed that the stitches should include all the coats of the vessel.

The actual technique is, then, as follows: The exposed vessel is clamped by some means, which must be very gentle, the simplest and best being, in my opinion, the clamp devised by Herrick.[17] Into the two ends of a piece of soft-rubber tubing are thrust two pieces of glass rod until the central ends touch. If the glass rods are now brought side by side a clamp is formed, the strength of which can be regulated to suit the occasion by clamping the free ends of the tubing with a hemostat. The loose connective tissue of the external coat of the vessel must then be dissected away, the best procedure being to draw it down over the cut end of the vessel and to snip it off even with the vessel end; it will then retract, leaving the vessel free. This must be done, else the loose tissue will interfere by being dragged with the suture into the needle holes. All insult to the vessel wall, such as grasping it with forceps, must be religiously avoided. If the edges of the wound have been crushed

they should be freshened by resecting a bit with a very sharp scalpel. Since the cut of scissors is always a crushing cut, they should not be used.

Three tension sutures of fine silk, impregnated with vaseline, are then laid at equidistant points of the circumferences of the vessel ends. An assistant applies traction to two of these guide sutures in turn, stretching the portion between the two sutures into a straight line, facilitating the laying of the continuous suture and preventing a narrowing of the lumen. If at this time the third tension suture is weighted by means of a hemostat, the circumference of the vessel will be arranged in the form of a triangle, the points of which are determined by the three traction sutures, and there will be no danger of catching the opposite wall while laying the suture. The suture is a continuous, overhand stitch, through all coats; the separate stitches should be drawn just tightly enough to secure absolute approximation, but not so tightly as to evert the edges; they must be laid very close together. After the completion of the suture and the removal of the clamps there will often be some hæmorrhage; if this is too free a few interrupted sutures may be laid, but a considerable hæmorrhage will almost always stop under gentle digital compression. I wish to emphasize this fact, because of its bearing upon the later theoretical discussion. The danger of aneurism formation is very small; secondary hæmorrhage is also rare.

The second method of end-to-end anastomosis is also accomplished with the aid of three tension sutures exactly as in the method I have just described. The edges of the wound are everted and the eversion is maintained by laying either interrupted mattress sutures, or a continuous mattress suture, or even by a running overhand stitch which is tightly drawn. The thinness of their walls makes it appear probable that this method must of necessity be used in the end-to-end anastomosis of veins. The method of invagination is accomplished by placing at three equidistant points of the proximal end, in the case of arteries, of the perpipheral end of veins, sutures armed with a needle at each end. These needles are then passed side by side from the interior of the vessel through its walls, at a little distance from the edge of the wound. The free end of the vessel is then fastened to the invaginated portion of the other end

by a series of sutures which do not penetrate all the coats of the vessel.

The use of a mechanical aid, as in the method of Payr,[8] consists in the employment of a little tube made of some absorbable material; Payr recommended magnesium for this purpose. The technique is precisely the same as that described for direct transfusion. By this method broad surfaces of endothelium are placed in contact and not even the finest needle holes are made in the intima; the cut edges of the vessel, exuding tissue coagulins, are entirely outside the vessel lumen. The method does not appear, however, to have given especially good results, except in temporary anastomosis, as in transfusion.

Now this sounds very easy, and, in truth, it is not very difficult, except for the extreme delicacy of the needles and the silk, and of the vessel walls; it is unusual surgery, since it partakes of the art of the watchmaker. Why, then, cannot everybody succeed in performing these simple, though delicate operations? Why do we read reports varying between absolute failure and uniform success? Why, out of four operations on the vessels of the neck of the same animal, do we sometimes find the arteries perfect, the veins thrombosed, or the veins patulous and the arteries closed, or only one success, or all failure, or all success? This is the question which, I think, leads us far away, into the fields where fact and theory too often establish a circulus viciosus.

In the first place, every author since Jassinowsky,[18] whose work formed the first real contribution to our knowledge of this subject, has emphasized the necessity of a perfect aseptic technique. Carrel goes so far as to express his opinion that under ordinary "aseptic" conditions there are always a few bacteria which gain entrance to the wound; now these are so few that in ordinary operations the tissues are able to destroy them. Not so in blood vessel surgery,—here we must have "absolute asepsis." Watts agrees with this opinion.[15] It may be hair splitting, but remember that this is fine work, I object to any further qualification of a word made by pasting an *a*-privitive before a noun. We must have asepsis, no sepsis, no bacteria, but this demand is not peculiar to blood vessel surgery.

That infection around an uninjured blood vessel will cause

thrombosis is banal. But I cannot believe that infection is the cause of the frequent thrombosis after blood vessel suture for several reasons; first, we find thrombosis with none of the usual macroscopic signs of infection; and secondly, an early examination will show small non-occluding thrombi, and older specimens will show such thrombi completely organized; in the third place, an infection would more likely have caused occlusion, being a progressive process. I have often observed that a thrombus will form in a sutured vessel, especially a vein, within a few moments after the clamps are removed, certainly hours too soon for these few bacteria to have caused it. Further, if this thrombus be removed by gently "milking" the vessel, another thrombus will replace it. In other words, the causes of thrombosis lie nearer at hand than bacterial action.

Just what happens when a blood vessel is wounded? The final processes of repair have been studied sufficiently to enable us to say that the vessel wall is completely repaired. The wound of the interior is covered with proliferated endothelium; some elastic fibres may regenerate, though the elastica is possibly not as perfectly repaired as are the other coats; the external coats are reconstructed by that excess of reaction so common in Nature as to be universal, and the vessel wall becomes stronger at that point than it was before the injury. The answer to my question must be sought in the work of men who delve deep in Nature's secrets and express their thoughts in unfamiliar language; we pass from "sutures" to "thrombokinase."

The problem of the coagulation of the blood is an extremely complex one. We know various factors in the process; we know that foreign bodies and roughenings of the intima favor coagulation; that an interference with the free current of the blood is a favoring factor. We know that the tissues contain a substance or substances which cause rapid coagulation of the blood plasma, and that these substances are present in the tissues of the vessel wall. The formed constituents of the blood also contain these same or analogous substances. Calcium salts are necessary for the formation of fibrin. Experiments upon the vessels of animals whose blood had been made incoagulable by injections of hirudin or of peptone have shown that another process enters into the play, an agglutination of the blood plaques or platelets.

It is not necessary for us to decide between the theories concerning what happens first, or what happens further, as whether the action is a ferment action or not. Let us think of the action of some of the factors in coagulation which I have mentioned.

The suture, being inelastic, must offer a point where the current of the blood is more or less influenced; the sutures are the foreign bodies; the holes in the intima are rough; the tissue coagulins contained in the vessel wall have access to the blood through the needle holes; blood platelets are deposited in the wounds of the intima, even in incoagulable blood, and we know that a true coagulum can start from such a deposition of platelets. Further, if two factors are united in these biological phenomena, the result is usually much greater than the sum of the separate action of each factor.

That some coagulation occurs in every case seems to me to be proven by the statement to be found in every report of extensive work,—that slight hæmorrhage is to be controlled by gentle digital compression. Such a method could only stop hæmorrhage by favoring the filling of the needle holes with a coagulum.

I therefore think that those who report uniformly successful results have succeeded not because they enjoy a monoply of aseptic technique, but of mechanical technique. In other words, the man who will master the numberless details of asepsis in experimental work upon animals, where matters are more complicated than in human surgery, is probably the man who will master the delicate mechanics of the operation. The vessels are brought together with the least possible stretching or narrowing of the lumen, thus affecting the blood stream as little as possible. The foreign body is made less active as a foreign body by impregnating the silk with vaseline. The silk is so chosen as to fill the holes made by the needle and thus prevent the admixture of tissue coagulins from the vessel wall. Having excluded these factors, the deposition of blood platelets, which, I believe, always fills the wound of the intima at least, may perhaps be insufficient to cause the formation of fibrin, and thrombosis.

It may not be out of place here to mention an operation which has never been of practical application, though its experimental use has borne fruit. It is the oldest operation on the blood vessels with consistently successful results. In 1876 a Russian army surgeon,

named Eck,[19] conceived the idea of making an artificial opening between the portal vein and the vena cava, in order to relieve the congestion in the portal system in cases of cirrhosis of the liver. He not only conceived this idea, but executed it experimentally; and since that time the operation has been often performed, yet in no report do we find that thrombosis or embolism resulted.

The operation has been done in several ways, none of which is calculated to prevent thrombosis. The vessels are brought together by means of interrupted sutures; wires or threads are then placed in position in the lumen of each vessel, so that when the small scissors, the blades of which are fastened to the wires, are drawn through, after a second row of stitches has been laid, each blade must cut a linear incision through the wall of its respective vessel, an incision limited by the points of entry and exit of the guiding wires; the line of this incision is then enclosed by a second row of interrupted sutures, parallel with the first, and the scissors are pulled through between the two rows of sutures. In my own method[20] the wire of an electro-cautery is substituted for the scissors. The portal vein is then tied off at the hilus of the liver, thus forcing all the blood through a torn or burned wound through all the walls of the veins. The interrupted sutures also pierce the intima.

We have, then, a beautifully torn, rough wound, sutures with no attempt to neutralize their action with vaseline, undoubted coagulation, since we have no hæmorrhage between the sutures, which are laid from one-sixteenth to one-eighth of an inch apart, and yet no thrombosis. The explanation may be that the portal vein has no collateral branches to open and enlarge, and the blood is forced to pass through this artificial opening; but, on the other hand, the pressure cannot be so great as it is in an artery. It might be that the portal blood contains peptone-like bodies, which inhibit coagulation, but this is hardly probable, for the portal blood coagulates outside the vessel as rapidly, if not more rapidly, than does blood from any other vessel. I have thought that the burned wound made by my cautery sealed the edges so that the tissue coagulins could not exude; yet equally good results have been obtained by using scissors; further, I have attempted to prove my idea by cutting the vessels of the neck with the cautery, and then joining them according to various methods. The results are possibly not so good as after the

vessel wall had been severed by a sharp scalpel. In short, I am willing to admit that the processes governing thrombosis are not sufficiently clear to my own mind.

For the practical surgeon I feel that we may draw these conclusions: In any case where the anastomosis of a blood vessel is indicated, it should be tried; aneurisms and secondary hæmorrhages should not occur. If immediate thrombosis occurs we would be as well off as though the vessel had been ligated; if gradual thrombosis occurs we might well hope that such a process would be more favorable to the formation of a collateral circulation than would immediate ligation.

The transplantation of organs is a problem which arises first after a successful method for anastomosing blood vessels has been elaborated. This field naturally falls into two distinct headings,—the transplantation of segments of blood vessels, and the transplantation or reimplantation of organs and limbs. Experiments upon the transplantation of segments of blood vessels began in 1896 (see [15], probably before that date, see [22]). I have not found any reference to this idea having been applied in human surgery; experiments have shown that it is possible to perform such a transplantation, and even to transplant segments of blood vessels from one species to another. Segments of veins have been made to assume the function of arteries, and their walls become thickened.

An operation belonging to this category has been tried several times upon the human being,[21] the anastomosis of an artery to its corresponding vein, as, for instance, in cases of gangrene of the extremities. Gluck, in 1898,[22] first succeeded in performing this operation experimentally. It is too early, I think, to decide just what we can expect from this operation. An enthusiasm greater than mine is necessary to carry one along the paths of reasoning according to which the reversal of the circulation will be the future treatment of goitre, for example.

A further possibility of blood vessel surgery is the operation of cutting down upon an embolus in either artery or vein and removing it, with subsequent repair of the vessel. This has been attempted in human surgery,[23] [24] and offers, possibly, one of the best opportunities for the successful surgery of blood vessels, since longitudinal wounds are most easily and successfully repaired.

Entire organs have also been transplanted experimentally, with most remarkable and encouraging results. One of the most recent and successful examples is reported in the following words:

"Both kidneys from a cat were extirpated and immediately replaced by both kidneys from another cat.

"After this operation the animal urinated abundantly. Urine collected during the first few days contained albumin. On the fourteenth day, the cat was operated on for hernia of the small intestine through the abdominal wound. The animal died from general peritonitis one day after this second operation.

"The anatomical specimen shows that the kidneys are a little enlarged. There is a slight hydronephrosis on the left side. Nevertheless, both organs appear to be in good condition."[25]

The work upon immunity, etc., above mentioned, which grew out of the problem of transfusion, proves conclusively that the somatic cells can no more be transplanted than can the cells of the blood; transplantation from one species to another is therefore out of the question.

The mere mention of the well known successful operations for the repair of penetrating wounds of the heart[26] closes the chapter upon the surgery of the blood vessels. The history of this chapter of surgery emphasizes one lesson in a peculiarly emphatic manner, the fundamental necessity of animal experimentation as the basis of surgical progress, and the value of cultivating it, not merely as a secondary feature of surgery, but as a basic art.

Neither the foregoing article nor the following list of references purports to be complete. I have touched upon what appear to me to be the salient features of the work at the present moment, and have given among the following references those which contain the most complete bibliographies.

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# INFLAMMATION OF THE GALLBLADDER AND GALL DUCTS

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Inflammation of the gallbladder and gall ducts varies in extent and intensity, being sometimes confined within the limits of the gallbladder, at other times extending to the cystic, the common, the hepatic, ducts and even to the bile ducts or radicles in the liver. It varies in intensity from a slight catarrhal inflammation to one which causes abscess, perforation, or gangrene of the gall bladder.

The causes may be divided into predisposing and exciting. Under *predisposing* causes are those conditions which tend to cause a deposit of the biliary salts and which produce stagnation by interfering with the normal flow of bile—such as a lack of balance between ingestion and assimilation, eating too much, drinking too much alcohol, in proportion to the amount of exercise taken; tight lacing, habitual attitudes which interfere with the bile stream; irritation from the presence of a foreign body, as gall stones.

Under *exciting* causes we have one chief, perhaps only, agent, namely infection from one of the pathogenic microörganisms, such as the typhoid bacillus, the staphylococcus, the streptococcus, the pneumococcus, the colon bacillus, and perhaps others, as the gonococcus and the influenza bacillus.

Stones are so frequently found in connection with these inflammations that the title "gallstones" is usually given to the disease. As to which comes first, the infection or the gallstone, is yet an unsettled question, though many believe that infection comes first and forms the nucleus of the stone—bacteria having been found in the interior of gall stones.

It is probable that stones form readily around any foreign material, as a blood clot or clump of cells, and that they act chiefly as a predisposing cause to infection, inasmuch as stones so fre-

quently exist without producing trouble. According to Kehr, 10 per cent. of the people in Germany have gallstones, but of these only 5 per cent. have symptoms from them—thus while 10 per cent. of the people have gallstones only one-half of one per cent. of the people, or one in 200, suffers from them.

Gallstones probably form most frequently in the gallbladder but they may form in any of the ducts—even in the liver substance, as in a case reported by L. L. McArthur at the Portland meeting of the American Medical Association in 1905, in which the liver substance was literally studded with stones of various sizes.

*Cholecystitis,* or inflammation of the gallbladder, may be catarrhal, suppurative, perforative, or gangrenous—depending on the kind of infection, the number of infectious organisms, and the resisting power of the tissues. It is not infrequently seen as a complication or sequel of typhoid fever, but it is also seen after pneumonia, grip, and other diseases. The typhoid bacillus may enter from the intestines directly by the common and cystic ducts, but it would seem that the hæmatogenous origin is more probable, as the germs associated with grip, pneumonia, and other diseases must enter the gallbladder through the bloodstream; besides we know that the blood contains the typhoid bacilli and that many organs and tissues do become infected in this disease, the pathway to which can only be through the bloodstream. The localization of the typhoid bacillus in various tissues and organs may thus lead to osteomyelitis, cerebral meningitis, neuritis, abscess of the spleen, etc.

The symptoms of cholecystitis are pain, tenderness in the epigastric and right hypochondriac regions, nausea and vomiting, chills, fever, and sometimes jaundice. In the *catarrhal* form the pain may be severe and resemble biliary colic, but there is not much tenderness or fever. In *empyœma* of the gallbladder there are pain, tenderness, chills, fever, sweats, and often vomiting. In *perforation* or *gangrene,* the symptoms may come on suddenly or after symptoms of cholecystitis, in the form of acute peritonitis or as a simple empyæma.

The diagnosis should be made from perforating ulcer of the stomach or duodenum, appendicitis, renal colic or ureteral obstruction, and intestinal obstruction. This is often difficult and some-

times impossible to do after peritonitis has set in. The following case illustrates catarrhal cholecystitis:

A female, aged 47 years, had been troubled with her digestion for several years. Had had several operations for lacerated perineum. During the past month the "indigestion" has become worse with attacks of violent pain in the epigastric region coming at short intervals, little or no tenderness to pressure, slight icteric hue of skin, light colored stools, anorexia, nausea, and slight fever —99 to 99.6. Diagnosis was made of the obstruction of the common duct. At the operation the gallbladder was found tightly distended and so much elongated as to resemble a sausage. Contents were mucus. No stone was found in the gallbladder, cystic, or common ducts. Cholecystostomy was done and was followed by free discharge of bile, relief of previous symptoms, and the formation of a biliary fistula which was closed five months later by a slight operation under cocaine. The patient continued to have some uneasiness in the gallbladder region and about two years after the first operation she had the gallbladder removed by another surgeon with relief of the symptoms.

Remarks: I did not remove the gallbladder at my first operation (1) because I was afraid there was a stone or some other obstruction in the common duct and I wanted the gallbladder for drainage; (2) the gallbladder was little if at all diseased, but distended, and since there was no sign of pus or infection, it seemed that if the obstruction which I could not find but which probably existed in the cystic duct, could be removed, the gallbladder would probably return to its normal state.

### CHOLECYSTITIS—PERFORATION—CHOLECYSTOSTOMY

The following case is a good example of perforation of the gallbladder probably from ulceration:

A man, 78 years old, who had been in good health except for some annoyance on account of a stricture of the urethra, was taken with severe pain in the right side, in the region of the liver and gallbladder. After several of these attacks he was suddenly taken with the worst attack he had even had—severe pain, vomiting, constipation, swelling of the abdomen, and fever, temperature 104°.

Examination 3 days later, August 26, 1905; there were vomiting, fulness, rigidity, and tenderness over the liver and gallbladder. Diagnosis: cholecystitis with suppuration. The abdomen was opened through the right rectus muscle with the escape of probably 1000 c.c. of thin, pale, green fluid containing flocculi of lymph, from below and above the liver. Patches of lymph were found on the diaphragm, liver, gallbladder, and colon. The gallbladder was distended, the coats thickened, and, on being separated from its adhesions, a patch of lymph was found near the neck, covering an opening where evidently the rupture had taken place. The gallbladder was opened at the fundus, evacuating mucus and bloody pus, the edges stitched to the abdominal wall, a rubber tube put in, and a piece of iodoform gauze below the gall bladder. The abdomen was then closed except the space about the tube and gauze. Uninterrupted recovery followed after a discharge of bile through the gallbladder for two months.

Remarks: This case shows the wonderful power of the natural reparative forces in the body, in closing without aid the opening in a ruptured gallbladder. This patient *might* have recovered without operation. The peritonitis was limited and was of the plastic variety. The cause of the rupture was probably an ulcer which may have been caused by a stone. The several attacks of pain which the patient had suffered previous to the last one indicated cholecystitis or gallstones—one or both. The stone may have escaped into the peritoneal cavity where it was lost. No stones could be found in the ducts and there was no jaundice. The gallbladder was not removed in this case for the same reasons that the appendix is not removed in some cases when the abscess is opened—because in doing so, barriers would be broken down, infection might be extended, the operation prolonged, and the patient's life placed in greater danger. In this patient Ransohoff's sign (yellowness of the thin skin of the navel) was sought but could not be found.

### PERFORATION OF THE GALLBLADDER IN TYPHOID FEVER

The next case illustrates the symptoms after perforation of the gallbladder in the course of typhoid fever.

A man, 26 years old, was ill with typhoid fever six weeks and

had had some tenderness over the gallbladder from the beginning. He also had several chills and a fluctuating temperature—nearly normal in the morning and high in the afternoon. Suddenly he was taken with severe pain in the gallbladder region, vomiting, rapid pulse, and higher temperature (104°). Three days later he was in a semicomatose state, delirious at times, abdomen distended, tympanitic and tender, pulse 110, and temperature 102. The diagnosis was general peritonitis from rupture of the gallbladder or intestine. Under cocaine the abdomen was opened through the right rectus muscle in the region of the gallbladder. On breaking up the adhesions with the finger there was a discharge of green fluid with flocculi of lymph. The patient's condition did not justify further operation, so a rubber drainage tube was inserted and the wound was closed. Death occurred 3 days later. The necropsy showed a perforation of the gallbladder.

Remarks: Cholecystitis is by no means unusual as a complication of typhoid fever, and perforation probably occurs more frequently than reports would indicate. Erdmann, in 1905, collected 34 cases of such perforation and reported one of his own. The condition may be confused with intestinal perforation, and as is well known, the septicæmia of cholecystitis or cholangeitis has been mistaken for typhoid fever. The diagnosis can usually be made by the character and location of the pain and often by the occurrence of chills, sweats, and widely fluctuating temperature. In the case reported, cholecystitis evidently existed from the beginning and the patient should have been operated on when the chills and fluctuating temperature appeared, in spite of the presence of typhoid fever.

### ABSCESS OF THE LIVER FROM CHOLECYSTITIS

The following case of abscess of the liver evidently had its origin in cholecystitis:

A married woman, 54 years old, had been suffering for a month with pain in the region of the liver, daily chills, and fever (99°, 102°, to 104°). No history of malaria or dysentery. On examination, a tumor, slightly tender but not fluctuating, was found four inches below the ribs on the right side and continuous above with the liver. An incision through the right rectus muscle,

over the tumor, exposed the outer or upper surface of the liver which extended downward in a tonguelike prolongation. The under or internal surface of the liver was adherent to the intestines in a mass and these adhesions were not disturbed. There were no adhesions on the external surface although fluctuation existed, so the liver was stitched to the abdominal wall around the fluctuating area, about one inch in diameter, the wound around the periphery was packed with gauze and a trocar and cannula thrust into the abscess, evacuating about 250 c.c. of thick, creamy pus. The opening was enlarged with hæmostats and a rubber drainage tube put in. At the end of two weeks pus had ceased to discharge and bile had taken its place. A probe passed up in the direction of the gallbladder for about four inches. This fistula continued to discharge a little bile and mucus at intervals for two years and then permanently closed. In the meantime the patient was in good health and was only troubled by the necessity of wearing a dressing over the fistula.

Remarks: Previous to operation this was thought to be a case of simple abscess of the liver. In the light of the operation it was decided best not to break up the adhesions in order to remove or drain the gallbladder, and later when a fistula had been established the patient was not willing to undergo another operation for that purpose.

*Cholangeitis,* inflammation of the gall ducts, when extensive or intense is much more serious than cholecystitis. It is caused by infection which is often secondary to cholecystitis, and is usually determined by the presence of stones in the common duct. The patient often gives a history of several attacks of biliary colic without jaundice (stone in gallbladder and cystic duct); then of attacks followed by temporary jaundice (stone floating in the common duct—ballvalve stone of Fenger); then an attack followed by permanent jaundice which may at times fade slightly or become more intense (stone impacted in the common duct). Chills and fever are common, with enlargement of the liver, and tenderness in the epigastric or right hypochondriac regions. Jaundice persists, the skin being sometimes bright yellow, mahogany, or intermediate in color. Death may be caused by abscesses in the liver, gallbladder, or septicæmia. The gallbladder is usually contracted, probably

because of the cholecystitis which existed previous to cholangeitis —while in cancerous obstruction, the gallbladder is usually dilated. Courvoisier's law may be shortly stated thus: A contracted gallbladder, with changing jaundice and pain, means stone in the common duct; a distended gallbladder with unchanging jaundice, without pain, means malignant disease or tumor interfering with the common duct.

### CHOLECYSTITIS, CHOLANGEITIS, CHOLÆMIA, MENTAL DISTURBANCE

The following case is a good example of cholecystitis and cholangeitis, illustrating one proposition of Courvoisier's law and the serious effect of cholæmia:

A man, 51 years old, had been "bilious" for several years and during the last two years he has had several attacks of severe pain in the epigastric region with vomiting and intermittent jaundice, chills, and fever. Four months past he had a severe attack, jaundice came on, and has continued ever since. For a month he has been in a semidelirious condition—conversing intelligently for a while and then almost imperceptibly wandering away into delirium. On examination slight rigidity and tenderness were found on the right side of the epigastrium, patient deeply jaundiced, pulse 90 to 120, and temperature 98° to 100°. A diagnosis of stones in the common duct was made.

Operation revealed a black, swollen liver, shrunken gallbladder which contained 18 small stones, and common duct much dilated. Cholecystostomy and choledochostomy were done, the stones removed, and rubber tubes put in. Through the opening in the common duct a probe was passed up to the liver and down into the duodenum without detecting a stone. Whether the stone had fallen back into the cystic duct, escaped into the intestine, or the probe failed to strike it in the ampulla of Vater could only be conjectured. There was no doubt that the common duct had very recently been obstructed. There was a free discharge of bile externally for six weeks, soon after which the wound healed, but the patient's mental condition did not become normal until four months after the operation. He had no recollection of the operation and did not remember any events for a month previous.

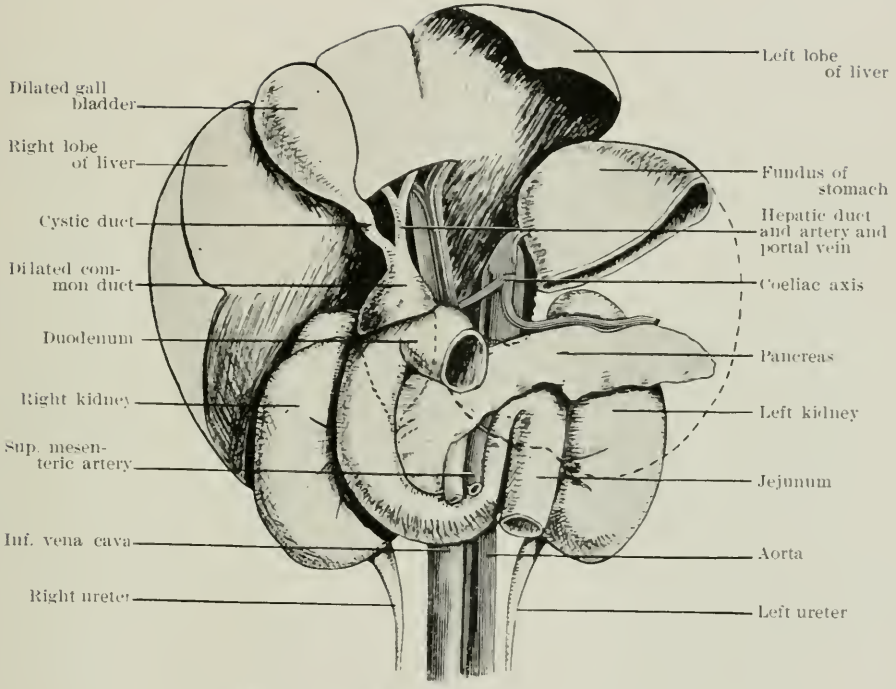
GALLSTONES IN THE COMMON DUCT WHICH WAS ENORMOUSLY DILATED—CHOLANGEITIS, CHOLEDOCHOSTOMY, DEATH ON THE 20TH DAY FROM HÆMORRHAGE

This case is an exception to Courvoisier's law in one respect, as the gallbladder was found dilated.

A woman, 40 years old, for several years had suffered from "indigestion" and pain in the right hypochondrium, having spells with pain, fever, vomiting, chills, and jaundice, lasting several weeks, then disappearing to return after a month or so. For three months she had been suffering almost continuously with pain in the epigastrium and occasional vomiting. During that time jaundice has been pronounced with yellow skin and conjunctivæ, dark colored urine, and putty stools. A diagnosis of obstruction of the common duct with gallstones was made and operation advised. No tumor could be felt but the right rectus and other muscles in the epigastric region were strongly resistant to pressure and after placing the patient under ether, a mass could be distinctly felt and seen in the epigastrium a little to the right of the median line.

On making an incision through the right rectus, a fluctuating, nearly round, swelling about the size of a croquet ball was at once seen between the liver and duodenum in the site of the common duct. The gallbladder was dilated and distended but showed no sign of inflammation. With the fingers in the foramen of Winslow two or three hard lumps could be felt in the head of the pancreas. The swelling was the enormously dilated common duct, extending from the cystic, down to within an inch of the opening in the duodenum and had a capacity of at least one pint. It was firmly adherent to the posterior part of the duodenum. It was opened and more than a pint of bile, pus and calculous material was evacuated, together with two small hard calculi, about ⅓ of an inch in diameter, which might easily have plugged the lower end of the duct. The gallbladder emptied itself and a probe was easily passed into the duodenum. The hard nodules in the head of the pancreas were examined carefully and one of them was incised. The opening in the duct was stitched to the anterior abdominal wall with catgut, a rubber tube put in, and

Fig. 1.




Case of enormously distended common bile duct.

a gauze drain a short distance below the tube, and the abdomen closed.

Bile was discharged freely after the operation and the patient seemed to be doing well for five days when she again began to complain of pain in the stomach and back, and of nausea. She was nervous and restless at night, requiring morphia. The bile looked thin, green, and contained flocculi. It was examined and tested by Dr. Reid Hunt, who stated that it consisted in large part of pancreatic juice.

Sept. 21st, the first hæmorrhage occurred—a considerable flow of venous blood from the lower opening.

Sept. 22nd, another similar hæmorrhage occurred and the opening was tightly packed with gauze.

Sept. 24th, death occurred at 8 P.M.—evidently from hæmorrhage. The annexed drawing by Dr. Paul Johnson gives a pretty correct idea of the condition.

Remarks: This may have been an instance of hæmorrhage on account of the cholæmia, but I am inclined to believe that it was caused by the giving way of some of the veins in the head of the pancreas—possibly from the action of the pancreatic juice. At the operation the head of the pancreas was incised and there was considerable bleeding, but this was finally arrested. In several cases of deep chronic jaundice I have had no trouble on account of hæmorrhage, except from that which might naturally follow injury to some of the numerous bloodvessels of this region.

In thinking over this patient as to how I might have done better, I have concluded that a cholecystenterostomy was the proper operation. The common duct was enormously dilated and already firmly attached to the posterior wall of the duodenum, so that it would have been necessary only to open the duct and intestine and stitch the anterior lips of the wounds together. This would have done away with drainage externally, would have insured the passage of the bile and pancreatic juice into the intestine, and in all probability would have prevented the occurrence of hæmorrhage.

In the *treatment* of cholangeitis the most important indication is drainage—drainage of the ducts, liver, and gallbladder. Usually this may be done best by opening the common duct and

gallbladder. The question of when to remove the gallbladder is one of importance. In this respect the gallbladder has often been compared with the appendix, and while there are points of resemblance there are very important points of difference. Removal of the gallbladder and ligation of the cystic duct may interfere with drainage in cholangeitis, or take away a convenient means of establishing drainage externally or into the intestine. The appendix can be put to no such useful purpose, except rarely in cases of colitis when appendicostomy may be required. Unless the gallbladder is gangrenous, the seat of malignant disease, or almost destroyed there is always some question as to the propriety of removing it. Suppuration is by no means an invariable indication for its removal. If we were certain, in a given instance, that there was no cholangeitis, no stone in the ducts or obstruction to the common ducts, removal of the gallbladder might be considered, but these are conditions often difficult, sometimes impossible, to determine.

# PERFORATING ULCER OF THE FOOT, ITS ÆTIOLOGY AND TREATMENT*

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The perforating or round ulcer of the foot, the "*mal perforant du pied*" of the French, is as its name implies, a round ulcer which perforates the tissues of the foot. That the lesion is rare is evidenced by the fact that some comparatively recent text-books on surgery make no reference to it; that its ætiology has not been established we are convinced when we see the pathologist dismiss the subject with a few vague references to spinal or trophic lesions, and the syphilographer publish a voluminous work without mentioning the lesion; that the proper treatment is still a matter for earnest investigation anyone will admit who has seen the ulcer recur in a patient who has been disfigured and maimed by surgical interference.

Believing that they offer valuable suggestions as to the ætiology and treatment of this condition, I submit the histories of the following cases.

Case.—(Figures 1 and 2.)—Mr. A., white, aged 65, an old soldier, acquired syphilis at the age of 21. The initial lesion and its sequellæ were successfully treated and he enjoyed vigorous health until 1902, when an inflammatory condition appeared at the metatarsophalangeal articulation of the right great toe. An abscess developed, was allowed to open spontaneously, and when a surgeon was finally consulted the joint was exposed. After a short period of tentative treatment, amputation of the toe was advised and the operation was performed, the wound healing kindly. The following year a similar inflammatory process involved the same joint of the left toe, and when the patient presented himself to another surgeon the bones and joint were involved to such an extent that it was thought advisable to amputate the toe and the first metatarsal bone. In 1904 an abscess formed on the right foot over the third

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* Read at the annual meeting of the Medical Society of Northern Virginia.

tarso-metatarsal articulation and another over the second phalangeal articulation of the third toe. These abscesses discharged, leaving ulcerating surfaces and sinuses which led to exfoliating bone. The ulcer on the foot rapidly deepened and soon made its appearance on the sole of the foot. At the same time an abscess, followed by ulcer and sinus, developed on the left foot over a tarso-phalangeal joint, and in a short time had perforated to the sole. At this time the case came into the hands of Dr. Kolipinski, who succeeded in obtaining a history of syphilis, a condition which had heretofore not been thought of. He at once began the internal administration of iodid of potash, and strapped the ulcers with mercurial plaster; a foot bath of hot bichlorid solution was used once daily. Under this treatment the patient, who had been confined to bed for several weeks, began to improve in health, the ulcer of the right foot soon filled up and healed, as shown in the photograph, Figure 2, the ulcer of the left foot improved slowly, and, I am informed, is now practically well.

Case II.—A few days after securing the photographs of Case 1, I was asked to see Mr. S., white, aged 40, an old soldier, now employed as a janitor. At this time his feet presented the appearance shown in Figures 3 and 4. He gave the following history: While in the army, detailed as a baker, in December, 1894, a barrel of flour fell, crushing the great toe of the right foot and bruising the same toe on the left foot. There was delay about his coming under observation of the surgeon, and when he finally presented himself the right toe was gangrenous and was promptly amputated, the wound healing in four or five weeks. Shortly afterwards he was discharged on account of disability. The left toe attracted little or no attention until two years after his discharge, when an abscess developed, which discharged and exfoliated pieces of bone, finally healing spontaneously, with the result shown in Figure 3. The ulcer seen on the second toe of the right foot appeared before the left toe had healed, and it persisted until and after treatment was inaugurated by me, when it healed in about two weeks. Eighteen months ago the patient stumbled and bruised the toes of the left foot. An inflammatory process developed, an abscess formed and discharged, leaving an ulcer and sinuses from which scales of bone were thrown off. About four months after the

FIG. 1.

Case I. Before treatment.

FIG. 2.

Case I. Showing Effect of Treatment.

Fig. 3.

Appearance of Ulcers in Case II.

Fig. 4.

Appearance of Ulcers in Case II.

injury the ulcer appeared on the sole, and ten months later, when the case came into my hands, the feet presented the appearance shown in Figures 3 and 4. This man had, in addition, typical symptoms of a well-developed case of locomotor ataxia. No history of syphilis could be obtained. Believing that a large percentage of cases of locomotor ataxia are of syphilitic origin, and having the history of Case I vividly in mind, I did not hesitate to assume that the initial syphilitic lesion in this case had been overlooked or forgotten, and at once inaugurated the same treatment. During the next few weeks his general health improved remarkably, and the man, who had been almost bedridden, has since performed his functions as janitor with little or no inconvenience. The ataxia improved; the shooting pains in the limbs disappeared and the ulcer on the right toe healed promptly. The ulcer on the left foot improved more slowly, but after several months was filled in and practically well, when an abscess developed again, the foot took on a gangrenous appearance and was much swollen and very painful until the abscess discharged, when all traces of inflammation disappeared and the reparative process was again inaugurated. The ulcer is now entirely healed, and the patient feels that he is to all intents and purposes cured. The gangrenous condition just referred to had developed to such an extent that, I dare say, many surgeons would have felt justified in amputating at least part of the foot.

In view of the histories of these two cases, noting especially that the lesions were bi-lateral and recurred after surgical interference, I feel justified in assuming that their ætiology will be found in the antecedent syphilis or a co-existing tabes dorsalis with or without a venereal history; that surgical treatment, in the absence of well-defined gangrene, is not at all indicated, since it mutilates and cripples and gives no guarantee against relapse or extension of the lesion, and should therefore never be undertaken until after the efficiency of the above therapeutic measures have been thoroughly tested; that these cases will yield to potassium iodide internally if venereal infection is still active, or to other appropriate medication if the case be one of locomotor ataxia, and that in all such cases local mercurial antiseptics should be used, of which the best are weak corrosive sublimate (1 to 5000) baths and the official mercurial plaster.

# SOME SURGICAL ASPECTS OF TUBERCULOSIS

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Surgical tuberculosis is as important as medical tuberculosis though it is not so dramatic in its manifestations and its symptoms are not so well known to the non-professional public. The crusade against the ravages of tuberculosis of the lungs has recently attracted much attention on the part of sanitarians and public authorities, because the medical profession has compelled its widespread existence to be recognized and its infectious nature to be understood. It required many years of active work on the part of enthusiastic medical men to overcome the general inertia and the conservatism of their colleagues before the great importance of the control of this disease was fully appreciated.

The widespread interest which is now being evinced in the establishment of sanitaria and the publication of educational pamphlets have brought the main facts of tuberculosis as the cause of medical affections prominently before the eyes of laymen. Non-medical people should now realize that the bacterial cause of consumption of the lungs gives rise to many diseases recognized as of surgical importance.

Many persons do not know that the chronic swellings of the neck due to lymphadenitis, "white swelling" of the joints, hip-joint disease, spine disease, inflammation of the brain, peritonitis, cold abscesses and many other affections are often the result of infection by the tubercle bacillus.

Tuberculosis is an infectious disease due to the presence in the tissues of the tubercle bacillus. The disease is one of the infectious granulomata, like syphilis, actinomycosis, leprosy and glanders. The growth of the fungus causes in the structures of the body a chronic inflammation giving rise to small masses of granulation tissue. The surgical manifestations of these affections have long been known under the old name of scrofula. These

symptoms were formerly believed to belong to a peculiar constitutional vice, in which there existed an abnormal tendency to inflammations of unusual chronicity and in which the products of inflammation were not readily absorbed but underwent cheesy degeneration in the infiltrated tissues. It is now known that the lesions formerly called scrofulous are nothing but local infections with the tubercle bacillus. As a rule the infection assumes an infiltrated rather than a nodular form.

It should be remembered that the original infection usually gives rise to a single lesion, but this often becomes the focus from which infection occurs in other parts of the body by transference of the tubercle bacillus through the lymph or blood stream. An important feature of this process is the fact that the single original focus may remain inactive, or comparatively inactive, for many months before the infection is carried by metastasis to other regions.

Doctors should teach their patients that infection cannot occur unless the tubercle bacillus gains access to the body of the patient. The germ may enter through the skin or mucous membrane at a point where there is a wound in this defensive armor; it probably may enter through the mucous membrane in certain regions without any actual wound furnishing a portal of entry. The tissues of the patient furnish a receptive soil, if their normal condition has been deteriorated by slight injury, or by a general condition of the body lowering the tissue resistance to deleterious influences. In other words, the tubercle bacillus may do little harm, if the patient's body has a normal healthy resistance to the germ. Ill health, due to bad hygienic conditions, anxiety, or inherited feebleness, furnishes a soil in which the tubercle bacillus grows with great readiness. Slight injuries may enfeeble the tissues at one spot and thereby provide a good soil for the tubercle bacillus to grow in, if it be circulating in the patient's blood. An interesting fact long known to medical men, though only recently understood, is that slight injuries in persons of lowered physical tone are not infrequently the exciting cause of a local tuberculous disease.

The inhalation of dried expectoration, from patients with tuberculous lungs, is one of the most common methods by which the tubercle germ reaches the tissues of a human being. This

is the reason that tuberculosis of the lungs is comparatively common, while surgical tuberculosis, though by no means unusual, is less frequently seen. Milk from tuberculous cows in a similar way leads to the introduction of the tubercle bacillus through the mucous membrane of the digestive tract. The admission of the germ to a healthy body often fails to give rise to tuberculous lesions because the resistance of the tissues to its attack is sufficient to prevent its growth.

The practical deduction from these pathological facts is that prevention of surgical tuberculosis depends largely on maintaining a healthy condition of the tissues of our patients. It is particularly important that this be accomplished during infancy and adolescence. The tissues of adults are not so good a soil for the growth of the tubercle bacillus, and surgical tuberculosis is therefore not so frequent in those who have reached the third or fourth decade of life.

Fresh air, plain food, good water and exercise in the open air constitute the best protection that parents can give against the invasion of tuberculosis. The dust of our habitations is so full of dried material containing the tubercle bacillus that prevention of the admission of that germ to the respiratory and digestive mucous membrane is practically impossible in most civilized communities. We must insist, therefore, upon the maintaining of a high standard of tissue health as well as the sterilization of sputum and other infectious discharges supplied by tuberculous patients.

It is not unlikely that the tubercle bacillus, at times, gains access to the organism through the mucous membrane of the tonsils and through carious teeth. This makes it important that acute and chronic inflammation of the tonsils should be efficiently treated and that carious teeth should be filled.

To prevent autoinfection of the patient from local foci of tuberculous disease, it may be wise, at times, to cut out the infected tissue. This method of treatment is particularly available when the tuberculous process is superficial, as in tuberculous lymphadenitis of the neck.

In addition to the hygienic measures already mentioned, nutrition is often improved by friction of the skin, bathing, and the

administration internally of cod-liver oil, iodide of iron, tonics, stimulants, arsenic, iodine and other remedial agents.

Surgical manifestations of tuberculous infection require the same general line of treatment as that adopted in cases of pulmonary tuberculosis. There are, however, mechanical and operative problems to be met that are absent in the therapeutic management of tuberculosis of the lungs. Collections of puriform fluid, often called cold abscesses, are frequently found in connection with tuberculous disease of the joints. They become exceedingly large under certain circumstances; as for example, the so-called psoas abscess, containing a pint or more of fluid, which has descended by gravity in the sheath of the psoas muscle, from softened tuberculous deposits in the bodies of the vertebræ.

Similar abscesses are found in connection with caries of other bones. They are conspicuous in knee-joint and hip-joint disease, though they are not so large as when they occur as a result of caries of the spine.

Special pains should be taken by the physician to bring to the attention of his clients the fact that these diseases are all due to infection with the tubercle bacillus. They therefore require the general line of treatment already discussed. In addition, rest of the joint, protection from injury and evacuation of the tuberculous fluid are required. They are not true abscesses and should not be confused with the acute suppurative processes due to infection with pus germs. They differ from acute abscesses in being chronic in their progress, having no very active symptoms and showing no tendency to point. There is no heat of skin and no redness, though finally there appears a rounded purplish elevation, which fluctuates on pressure. Incision evacuates a thin fluid, of yellowish color, often containing cheesy masses and granular material. These puriform collections require evacuation with the aspirator; or incision, disinfection and drainage.

Enlargement of the lymph nodes is a common surgical affection due to tuberculosis. As is well known, the lymph nodes are filters which retain, from the lymph current going through them, bacteria and other particles floating in the stream. The arrest of the germs, in the sieve-like nodes, causes obstruction of the lymph current, coagulation of the lymph and a tuberculous inflammation of the

tissue of the node. This irritation may involve secondarily the surrounding tissues. As a result there is a nodular swelling due to the enlarged lymph nodes. These, after a time, may soften because of the degeneration of the cheesy tuberculous material in their interior. The neck is a common site for these tumors, formerly called scrofulous glands. The possibility of such tuberculous foci causing autoinfection of the individual must be considered, when it is necessary to decide as to operative treatment. It is not unusual for such masses to disappear under hygienic treatment combined with local stimulation by means of external application of iodine or mercury.

A more prompt recovery and less scarring will often be obtained by an early excision of the nodes than by waiting for spontaneous absorption. Softening of the interior of the nodes, after a long time has elapsed, is very common. The softened material is then discharged through openings in the skin. Many months often pass before these sinuses heal; and then puckered and irregular scars remain to mar the skin. Unless the disease is confined to one or two glands, which break down rapidly, it is often better to proceed to a formal operation and extirpate all the involved lymph nodes. By placing the incision in an inconspicuous place, it is possible to get rid of the tuberculous nodes promptly and have almost no cosmetic defect remain. Large masses may be removed from this region by making the incision in the hair, at the back of the neck, and turning down a large flap so as to uncover the infected glands. The growth of the hair will then hide the scar.

Tuberculous osteomyelitis is one of the most important conditions with which surgeons have to deal. It is the cause of hip-joint disease, spine disease and the inflammations of other joints, which used to be called white swellings. The inflammation of the bone is due to infection with the tubercle bacillus, and is similar to ulcerative processes in soft structures.

The pathological process is particularly apt to affect spongy bone, such as is found in the bodies of the vertebræ, the head of the femur and the short bones of the wrist and ankle. It is the softening of the tuberculous deposits in the bones of the spine that gives rise to the hunchback appearance, which is by no means infrequent among children subjected to unhygienic conditions of

life. Many laymen and perhaps some members of our own profession fail to realize the identity of the process which produces hunchback with that which is so destructive of the hip-joints of many little children.

I call particular attention to the fact that these hip-joint conditions are nearly always tuberculous, in order to lay stress upon the necessity of preventive treatment and careful management in the early stages. Both spine disease and hip-joint disease, if taken at the beginning of the process, may, in many instances, be cured by maintaining the nutrition of the patient, putting the joints at absolute rest, and preventing the deformity. The last comes when the bone is softened, if the skeleton is required to bear weight.

The great deformity of the back and chest, due to untreated or badly treated tuberculous spine disease, may be almost entirely obviated by putting the patient in the recumbent posture, so that the spine need not carry the weight of the head and shoulders. In the mild cases and in others, during some period of their progress, sufficient fixation of the spine may be accomplished by the application of a gypsum jacket, having the pelvis for the base of support. In a similar way the deformity, which results from destruction of the head of the femur, may be obviated by putting the hip-joint at rest at the beginning of the tuberculous invasion of the joint structures. Traction, with the patient in bed, or the wearing of proper splints, to prevent the weight of the body being carried on the affected limb, will often lead to cure with no other disability than a slight stiffness of the joint.

The medical profession has in some instances failed to recognize, however, that these important mechanical devices should be supplemented by life in the open air and good food. Many patients go from bad to worse, because the surgeon is more intent upon the mechanics and pathology of the disease than he is in maintaining the nutrition of the patient by fresh air and sunshine. It is possible, in nearly all instances, to give the patients the benefit of sunlight and fresh air by placing their beds in well-ventilated rooms, or upon roofs or open porches. This method of treating tuberculous cases has not been utilized in surgery as much as it should be. Tuberculous diseases of the lungs do not need such

hygienic management any more than do these surgical cases of caries of spine and hip.

Pyogenic infection is often combined with tuberculous infection, when the opening of puriform collections permits the access of pus germs from the exterior. The mixed infection, so produced, frequently leads to a pyogenic septicæmia which ends only with the destruction of the patient's life. The alert and wise surgeon will do his best to obviate this catastrophe, by the antiseptic dressing of open surfaces and the building up of the patient, by the means already referred to in this discussion.

Parents particularly should be on the alert for pain in the region of the intercostal nerves in young children. This is one of the early symptoms of tuberculous spondylitis or spine disease. Frequent attacks of stomach ache in little children and a constrained method of stooping with a rigid back bone should suggest the possibility of incipient tuberculosis of the spinal column.

Frequent pain in the hip or inner side of the knee, accompanied by alteration in gait, such as a slight limp, should make the parent suspicious of a possible invasion of the hip-joint with the tubercle bacillus. "Growing pains," so called, of children should sound the warning for a surgical examination by an expert observer, lest the best time for avoiding destruction of bone and much suffering should pass with the true nature of the disease unrecognized.

It is not my intention to lay stress in this lecture, on the therapeutics of surgical tuberculosis. It has been my wish simply to call attention to the widespread occurrence of lesions due to tuberculosis. It has become too much the custom to think that tuberculosis means disease of the lungs and nothing else.

In addition to the lesions, to which I have referred as due to tuberculosis, there are many other surgical conditions resulting from this infection. Ulceration of the face, known as lupus vulgaris, is a form of tuberculosis of the skin. The usual cerebral meningitis of childhood is an infection of the membranes of the brain with the tubercle germ. Peritonitis occurs quite often from the same infection and requires operative treatment. Ulceration of the mucous membrane of the intestines may be a manifestation of local tuberculosis. It may lead to cicatricial stricture of the gut

and consequent obstruction of the bowels. Tumor-like masses in the breast, the tongue and elsewhere may be of tuberculous origin and need operative removal. Tuberculosis of the kidney, the bladder and the genital organs of the male and female is quite common. Indeed the pathological conditions resulting from the growth of the bacillus of tuberculosis in a congenial soil are numerous and of the greatest surgical interest.

# Gynecology

## COLLARGOL IN PUERPERAL INFECTION

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The favorable effect of colloid silver, or collargol, in the treatment of infectious pyrexia could not fail to attract the attention of accoucheurs from the point of view of its application to the treatment of puerperal fever. The promoter of the use of this therapeutic agent, B. Crédé (1897), was the first to indicate its adaptability to the puerperal state.

The very complete article of Netter (v. Intern. Clinics, 14th series, vol. 1) made known the doses and method of use of collargol. We will here merely mention that the ways in which this remedy can be administered are many, and depend on the nature and acuteness of the infection, and whether the disorder is due to a localized or generalized infection.

If a slow, continuous and prolonged modifying action is indicated, collargol can be introduced into the system by the endermic method of inunctions repeated over a long period, or in small doses by the stomach, or even by the intestine in the form of enemas. But when an immediate and energetic effect is imperative, it must be administered by intra-venous injections.

As a topic the collargol can also be used in localized infection when the seat of the infection is accessible. By this means we have obtained results superior to those obtained by any other remedies in treating ophthalmia neonatorum.

The administration of collargol by hypodermic injection cannot be recommended. This method is inefficacious on account of the extreme slowness with which the substance is absorbed; the solution impregnates the cellular tissue and raises the skin, which turns quite black. Furthermore it gives rise to severe and persistent pain, which radiates through irritation of the nerve-threads. In

some cases the seat of the injection suppurates; a case was published in which extensive necrosis of the cellular tissue of the arm occurred. In the majority of instances of this sort the accident occurred, not after deliberate hypodermic injections, but after subcutaneous diffusion of collargol during an intra-venous injection badly done.

Collargol can be given by the stomach, either in a hydro-albuminous solution, or in pills of five or ten centigrams. We have never made use of this mode of administration.

The same solution (one per cent.) can be given per rectum, as has been done by Chrobak and Küstner in the treatment of puerperal fever.

For local use on infected surfaces a solution ranging from one to ten per cent. is employed. Personally, in treating purulent ophthalmia, we have obtained better results with a two per cent. solution than with those that are stronger.

Recently B. Crédé has recommended the local use of collargol in the form of suppositories introduced either into the vagina or into the uterine cavity as a preventive for puerperal infection. These suppositories he also advises, together with intra-venous injections or inunctions, as auxiliary means in cases where infection already exists.

Some obstetricians content themselves with painting the uterine cavity, as a curative means, with a collargol solution of from two to five per cent. We have tried this method, as we have also tried solutions of protargol before the days of collargol; but the results obtained did not appear sufficiently striking to prefer this technique to the method of intra-venous injections.

For inunctions, what is known as Crédé's salve is used; lard, 100; white wax, 10; collargol, 16. When the skin has been thoroughly cleaned with soap and ether, the proper amount of salve is slowly rubbed in for fifteen minutes or so. The amount advised by Crédé varies between one and three grams, but this quantity can be doubled or tripled.

We have used the inunction method on various occasions either to continue and reinforce the action of intra-venous injections already administered, or, as happened to us twice, because the superficial veins were not accessible on account of excessive fleshiness.

This is the process that Chrobak prefers. In the 73 cases reported by Buberl, Crédé's ointment was used 47 times, as against 13 for the intra-venous injection and 13 times in which the collargol was given both in enema and in inunction. Nevertheless we do not hesitate to accord this method of using collargol a distinctly second place when compared with the intra-venous injection. The latter can be made in any one of the superficial veins of either upper or lower limbs. At the Bucharest clinic the point preferred is the inner saphenous vein, above the malleolus, the vessel being first uncovered and freed.

In agreement with the great majority of writers, we prefer to operate on the veins of the upper limb, and so far as possible at the elbow. It has, however, happened to occur that we were not able to bring these veins sufficiently into relief by means of a ligature applied to the arm, either because they were small, or because they were buried in fat, as is common with women. To succeed with an injection in such cases, it is necessary to dissect out the vein, run a probe under it, open it with scissors, and, after the injection is made, apply a ligature. This is manifestly a small, painful surgical operation, requiring the use of instruments and necessitating more complicated antiseptic preparations than we now use. It was only when we first began to use collargol that we dissected out the vein. Nowadays we simply puncture the vessel through the skin by means of the needle of an ordinary hypodermic syringe. If no vein can be brought into relief at the elbow we take the cephalic vein above the thumb, or any one of the veins of the back of the hand. The operation itself is very simple. The collargol solution is taken up into a Roux syringe of ten to twenty cubic centimetres. A small india-rubber tube is then adapted by one end to the syringe, and by the other to the free end of the needle when the puncture has been made. The skin having been carefully cleaned, the vein is made prominent by applying an india-rubber bandage around the arm. The arm should be extended and held steadily. The left thumb is applied to the vein to keep it in place just above the point where the needle is to enter. The needle, held in the right hand, is run into the vein as obliquely as possible in the direction of the vessel, the appearance of successive drops of blood indicating that it is properly inserted. If these drops do not appear the operation must be

repeated higher up or lower down. The constricting band is then removed, the tube adjusted and the injection slowly made.

The accidents that may arise in the course of this little operation are air embolus and transfixion of the vein. We do not speak of septic contamination, for which the operator alone is to blame.

The risk of air embolus would seem, a priori, to be serious; for liquid preparations of collargol become frothy at the slightest shaking. To prevent this, it is necessary to fit the tube carefully onto the syringe and drive out every air-bubble; and, as a complementary precaution, to hold the syringe vertically while the operation is being carried out, and to stop before the liquid has entirely left the instrument.

We have only seen one case of air embolus reported, by Buberl, at Chrobak's clinic; but the accident had no special ill results.

Transfixion, or secondary tearing of the vein with the point of the needle, is fairly common and not easy to avoid. It occurs when the puncture is made, if the needle is not well pointed in the direction of the vessel or when it does not enter the vein sufficiently obliquely. The immediate appearance of a lump under the skin due to the escape of a certain amount of blood gives warning of this occurrence.

To avoid a tear taking place during the injection itself, it is advisable to have the arm tightly held, and to see that the needle, when once in place, receives no jerk from the movement of the piston; it is for this reason that we use a flexible india-rubber tube a few centimetres long between the syringe and the needle. Nevertheless, if in spite of all care, the vessel is torn, a lump forms at once. The injection must then be stopped immediately and begun again some distance away, to prevent the spreading of the collargol in the cellular tissue. We mentioned above the undesirability of this pharmaceutical thrombus.

The strength of the collargol solution to be used in intra-venous injections is between one and two per cent. The latter is advised by Crédé. More concentrated solutions do not appear to be more efficacious, and are perhaps not dangerous; the accidents reported by Baum (pulmonary embolus, extensive thrombosis of the vein, necrosis of the cellular tissue) were observed after injections made with a ten per cent. solution. Our own practice has been to use the

one per cent. solution, of which our average dose per injection has been ten cubic centimetres.

What way does collargol act on the fluids and cells of an infected organism? Crédé thinks that the action is simply that of an antiseptic or bactericidal agent. Netter thinks that this substance also acts, and chiefly so, by a catalytic power analogous to that of ferments. According to Wassmuth, the peculiar sensation of euphoria that follows a collargol injection in infected patients corresponds to an impregnation, a sort of poisoning of the entire system; the electro-catalytic power of the colloid metal gives rise, in his opinion, to rapid tissue-oxidation, resulting in destruction of the toxins.

A solution of collargol acts in vitro as an antiseptic. A. Pinto and Marquis dos Santos, repeating and completing the research-work published by Brünner, found that a streptococcus culture is destroyed by a few drops of a $^1/_{6000}$ solution, and that its development stops in a $^1/_{4500}$ solution. The same is true for the gonococcus, the golden staphylococcus, and the bacillus anthracis, although the latter has greater powers of resistance. These facts show that as a solution of collargol is antiseptic in itself, it does not have to be sterilized by overheating, a process which it would not bear well.

Proceeding to experimentation, the writers just mentioned found that collargol has the same inhibitory effect on infection in animals. A preventive dose of five milligrams per kilogram enables a rabbit to support the dose of a culture that would be ten times enough to kill it. When injected in similar quantities, after a streptococcic inoculation of a dose ten times fatal, it saves the life of the animal.

Collargol spreads very rapidly to all parts of the system. By means of experimentation, and by research on the cadaver, it is found to go chiefly to the liver, spleen, bone marrow, kidneys, intestines and lungs (Beyer). Like all colloid substances, its elimination is slower than that of crystalloid substances. The elimination takes place principally by the intestine (Beyer).

Its biological effect is to render blood-coagulation less rapid (Pinto and Marquis dos Santos). It occasions, in addition, marked leucocytosis, as has been noticed by all writers, which begins at once after an injection, reaches its height generally in about six hours, and disappears in twenty-four hours. This is a salutary reaction,

increasing the powers of defence of the system against bacterial invasion. Still, Majewski considers that the intra-venous use of collargol is dangerous; although hyperleucocytosis takes place, this is, he says, followed by destruction of polynuclears, the percentage of which falls in consequence below the normal; in addition, he claims that collargol has from the start a hæmolytic effect on the red blood corpuscles.

To these modifications of the blood correspond as clinical manifestations two symptoms: temporary increase of the pyrexia, and the appearance of a rigor.

Except when we have used this treatment as a last resort, with patients who were practically dying, this rise of temperature has always shown itself. It occurs one or two hours after the injection, and reaches its maximum after the rigor; it only lasts a few hours, and is followed either, in the most favorable cases, by rapid defervescence, or by defervescence in lysis, bringing the temperature down to the normal in from two to six days, if recovery is to be obtained by a single injection. On the contrary, when further injections are necessary, the rise of temperature takes place after each injection. This rise is sometimes considerable. It is not rare to see the temperature in the axilla reach and pass 106°. In one instance, which was followed by total defervescence in thirty-six hours, the temperature, taken twice within a few minutes, reached 108°. The constancy of this phenomenon does not enable us to attribute it, as Crédé does, to impurities in the preparation of collargol. This reaction can, as yet, only be explained by hypothesis.

Although less frequent, the rigor, which accompanies or precedes the rise of temperature and the leucocytic manifestation, is fairly regularly observed, particularly in favorable cases.

Personally, among forty cases of puerperal infection which we have treated by collargol, at Lariboisière Hospital, we have been struck by the relative frequency of the rigor in cases that recovered, and of its rarity in fatal cases. In 27 cases that ended in recovery the rigor was noted in 19, that is, in 70 per cent.; whereas it occurred only 4 times in the 13 cases that ended fatally, or 30 per cent. We are therefore warranted in attributing to this symptom a prognostic value of some importance. It was

absent in the case of some patients who recovered, when the injection was made immediately after a rigor due to the infection. It was always lacking in the case of women treated shortly before death.

A point worthy of note is that this rigor generally occurs only after the first injection, and not after those made subsequently. We have, however, observed it to be absent after the first injection, and to appear after the following one. Cases where it appears after each one of a series of injections are very unusual.

A third feature of the reaction, fully as common as the two foregoing, and to which the women all call attention themselves, is the very peculiar sensation of euphoria that comes over them after an injection; their distressing symptoms: headache, intense thirst, and dyspnœa, disappear very rapidly. This was quite striking, for it took place in one patient at the same time as the rigor, while the temperature in the axilla rose to 108°. The rigor apparently causes no more discomfort than that which follows normal delivery, and in this respect differs markedly from the rigors that accompany the previous state of septicæmia.

The accumulation of collargol in the system, in spite of its slow elimination, gives rise to no signs of argyria (paralysis, nephritis, enteritis, etc.), as is the case with argentum nitrate. And although the dose of ten centigrams which we advise seems to us harmless, we should hesitate to raise it to twenty-five, as Cohn recommends, particularly as the therapeutic results bear no proportional relation, in their degree, with the size of the dose employed. By means of a large and concentrated dose Beyer was able to give rise to thrombosis and pulmonary embolus in the guinea-pig. This accident has been repeated in practice, though very rarely. With one of our cases, a report of which was published in Legrand's thesis, pulmonary embolus, though without serious consequences, occurred two weeks after an injection of ten centigrams of collargol; and Osterloh and Courant have each published a fatal case of pulmonary embolus occurring several days after an injection.

In interpreting these accidents, while by no means attempting to deny the possible undesirable action of the collargol, we must not forget that similar accidents are not unusual in the puerperal state when no treatment by the veins has been employed, and that these complications may be attributed to septic emboli.

At the present time our experience has been sufficiently protracted to convince us of the harmlessness of the use of collargol in intra-venous injections, and of its curative properties from a clinical point of view.

When at the beginning we started to use this treatment, influenced by what B. Crédé had published, who presented it as a sort of specific for puerperal fever, we had just encountered a long series of failures with the use of Marmorek's serum. We had to abandon a means of treatment that seemed as rational as unfortunately it proved to be inefficacious, and the method we decided to try, on account of our insufficient knowledge of the mode of action of colloid silver, did not inspire us *a priori* with any more confidence than any other empirical remedy. But chance favored us. Our first trial, in January, 1903, was a very timid one; we injected two c.c. of a two per cent. solution in the case of a woman whose temperature kept oscillating between 100° and 104°, in spite of all our endeavors. Defervescence was sudden and immediate, and was only disturbed secondarily (100°) by the appearance of an abscess. Since that date, taking only hospital cases into consideration, we have collected forty complete observations, of which the first eighteen were published in Legrand's thesis.

Although this total, representing a period of four years, is not very considerable when we take into account the large number of cases of infection that pass through the isolating ward of a Maternity as busy as that of Lariboisière, cases of which the most serious if not the most numerous concern women brought to the hospital with an infection and often destined to die in a very short time, still the fact that the series of cases is so small is due to our desire, in order to acquire reliable statistics on the value of collargol, to reserve it, until quite recently, for the most serious cases, cases that resisted all our ordinary methods of treatment.

By acting on this principle we endeavored to guard ourselves against a twofold error in interpreting results: first, that of counting as successful recoveries cases in which the infection was slight and benign and might have almost recovered without treatment; second, that of attributing to collargol, by using it from the start, recoveries due to our usual treatment carried out at the same time. But we have not been able to eliminate altogether the latter source of error,

because although until lately we waited until the ordinary treatment failed altogether before resorting to collargol, we did not dare to set the former entirely aside to allow the collargol to act alone, except of course in cases where the favorable effect of the collargol began to manifest itself as soon as the first injection was made.

The results of our experience, which, owing to lack of space, we regret that we are not able to substantiate by the detailed publication of our cases, with their temperature charts, have been as follows: Out of 40 cases, 27 made favorable recoveries. In 15, recovery was obtained with a single injection; in 7, two injections were required; and in 5, there were made from three to five injections. Of this number 4 were cases that had not proved refractory, but that were grave from the start, and in which the collargol was injected at once and, in a certain sense, as a prophylactic,—women with a putrefied fœtus and fever during labor, or with fever and autocontamination through extra-genital suppuration.

Among the 13 women who succumbed, 9 received but a single injection, 3 of whom came to the hospital the day before their death as a last resource; 3 received two injections; 1 died after a long period of cachexia, in spite of five injections. As already stated, then, the proportion of recoveries with the collargol treatment reaches 70 per cent.

If we consider that in our Maternity the sick rate from autochthonous puerperal fever is hardly one in twenty, and that the death rate in the same conditions is from 2 to 3 per thousand, or 5 per cent. among infected women, it might be thought that the death rate of 30 per cent. which our statistics show for patients treated with collargol is far from pleading in favor of the therapeutic efficacy of this agent. For this reason we desire to lay stress on the fact that our first researches dealt almost exclusively with remarkably serious cases, women brought in from outside, with forms of septicæmia resisting all ordinary treatments employed in the first instance, and that in the majority of the cases we turned to the collargol as our last ray of hope.

# ATOPOMENORRHŒA

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AND

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Louisville, Kentucky

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The illustrious Bland Sutton is reported to have said before a meeting of the British Medical Association that "the idea of vicarious menstruation is an exploded superstition," which is presumed to mean that (in his judgment) such instances are totally unknown. *Per contra,* however, there is overwhelming clinical evidence from numerous conscientious and careful observers who have noted and recorded various types of the anomaly designated vicarious menstruation, and it seems extraordinary that the extensive experience of Sutton should not include the observation of a single case of this character.

Since from time immemorial there have been noted periodic sanguineous discharges (vicarious menstruation) from various extraneous organs and structures of the human female (and sometimes the male), it would appear a rank insult to professional intelligence to attempt to deny the occurrence of such anomalies; and there is abundant clinical evidence to substantiate the suggestion that such abnormal occurrences are not so infrequent as indicated by most modern medical text books.

Nearly every physician of ordinary experience has observed instances where there have been periodic hæmorrhages (identical with menstrual blood) from the nose, the lungs, the stomach, the skin, the rectum, the nipples, the breasts, the ears, the eyes, or elsewhere; and (*a*) as in typical cases the catamenia is usually absent, (*b*) the vicarious hæmorrhage recurs with more or less regular periodicity, (*c*) as investigation has proven that the abnormal discharge differs in no essential feature from menstrual blood, and (*d*) as it is more often than otherwise associated with the character-

istic phenomena which commonly precede and attend menstruation through the customary channel, if such instances be not vicarious menstruation will not Mr. Bland Sutton suggest some reasonable explanation of the facts to reconcile his dogmatic assertion that it may not be at distinct variance with clinical observations which have so often been repeated?

Case 1.—Miss G., aged sixteen, began menstruating regularly at the age of thirteen years. The flow was scanty and attended with constitutional disturbances sufficiently severe to keep her in bed for the first two days. Nausea, vomiting, pain in the head, back and pelvic region were the most prominent characteristics. At seven she had diphtheria, and later suffered from some of the other common diseases incident to childhood, otherwise her general health had always been excellent.[1] She was physically well developed and weighed one hundred and sixteen pounds. There was no abnormality of the genital organs, and her mammæ were the size which is normal at this age.

At fifteen years of age menstruation entirely ceased, and instead there occurred vicarious hæmorrhage from a large venous nævus situated on the left side of the face and neck, at the regular menstrual intervals and lasting two days, which presented every clinical appearance of menstrual blood. She continued to suffer pelvic pain and the other symptoms mentioned, necessitating her remaining in bed during each epoch, but there never occurred any further flow from the uterus. Various methods of treatment were instituted with distinctly negative results. At last accounts she was still living and there had been no change in her condition.

Case 2.—Another form of vicarious menstruation is aptly illustrated by the case of Miss C., aged thirty years, in whom the catamenia had never been established. She had always enjoyed good general health, and in all respects appeared normal except for a peculiar and unnatural greenish pallor of the skin, "transparency"

[1] According to Playfair this strange deviation of the menstrual discharge may be taken as a sign of general ill-health, and is encountered most often in delicate young women of highly mobile nervous constitution! This observation is certainly erroneous, or at least not borne out by facts, since it appears from cases reported that ill-health is the exception rather than the rule in those females who are the subjects of vicarious menstruation. Q. W. H.

of some authors, and the fact that she spoke with a faint, husky, or "whispering" enunciation, for which no reasonable cause could be assigned. She stated that these peculiarities had existed since her earliest recollection. She was a well developed woman, the breasts large and prominent, and there was present no sexual abnormality.

Since the age of sixteen years there had occurred vicarious menstruation from the mouth once a month unattended by any symptoms worthy of note except a feeling of general malaise. The blood was not vomited but proceeded from the mucous membrane of the fauces and the buccal cavity. The woman died about a year ago, the result of an intercurrent malady.

The literature of this subject contains many cases of more than passing interest: Lhéritier records an instance which has often been quoted, viz.: a young girl suffered from suppression of the menses, which, instead of flowing through the natural channel, issued periodically for four years from extraneous sources, first from vesicles on the leg, second from an eruption on the left arm, third from a sore on the thumb, fourth from the upper eyelid. An identical case is reported by B. de Boismont and Meisner, and Haller cites eighteen instances of menstruation from the skin. Parrot also mentions several similar cases, and Chambers speaks of a bloody perspiration occurring periodically in a woman of twenty-seven years.

Van Swieten reports what was probably vicarious menstruation from the eye following injury, and subsequently blood oozed from the skin of the nose and was said to run "in jets" from the skin of the fingers and also from under the nails.

D'Andrade cites the case of a girl eighteen years old who menstruated regularly from thirteen to fifteen and a half years, then the catamenia became irregular and there occurred occasional hæmorrhages from the gums and nose together with attacks of hæmatemesis. Menstruation returned, but later blood issued from healthy skin of the left breast and right forearm, recurring every month or two, and finally additional dermal hæmorrhage developed on the forehead. In other instances, recorded after ten years' suppression of the menstrual function, there appeared a discharge of blood from a vesicular eruption on the finger, and a prostitute

menstruated through "spots the size of a five franc piece" which developed on the breasts, buttocks, back, axilla and epigastrium.

Barham records a case in which menstruation assumed the character of periodic purpura, and Duchesne refers to a case of complete amenorrhœa where the ordinary flow was replaced by periodic bloody sweats.

Parrot cites the complicated case of a child who when seven months old suffered from strumous ulcers which left cicatrices on the right hand from which at the age of six there issued a sanguineous discharge, and once she shed bloody tears. She menstruated at eleven, and her condition seemed thereby temporarily improved, but strong emotion caused return of the vicarious hæmorrhage. On one occasion, after marriage, when the menses were delayed, she exhibited a bloody exudation from the forehead, eyelids and scalp. There were also occasional attacks of hæmatemesis.

Schenck reports instances of menstruation from the nipple; and Richter, de Fontechia, Laurentius, Marcellus Donatus, Amatus Lusitanus and Bierling, are some of the older writers who have observed this anomaly. Paré refers to a woman who menstruated so copiously from the breasts each month that "several serviettes" were necessary to receive the discharge.

Cazenave has observed mammary menstruation with bloody exudation from the face, and Wolff saw an example associated with hæmorrhage from the fauces. A case of monthly discharge of blood from beneath the left mamma is reported by the Lancet. Finley also cites an example of mammary menstruation, and Barnes saw a young girl who menstruated vicariously from the nipple and stomach. A case is recorded of a woman aged fifty, never pregnant, the menopause having occurred two years previously, who for twelve months had menstruated regularly from the nipples, hæmorrhage being sufficiently profuse to require frequent change of napkins.

Boulger mentions an instance of periodic menstruation from beneath the left breast,[2] and Jacobson speaks of habitual menstrual discharge from both mammæ. Rouxeau saw a girl of seventeen suffering from amenorrhœa who menstruated from the breast, and

[2] This may be the same case accredited to the Lancet, q. v. Q. W. H.

Teufard reports a case in which there was re-establishment of menstruation (from the mammæ) at the age of fifty-six years. Baker gives an instance of vicarious menstruation from an ulcer on the right mamma in a woman of twenty who had never menstruated regularly or freely.

Bellini, Hellwig and Dodonæus speak of menstruation occurring from the eye. Jonston also gives an example of ocular menstruation, and Bartholinus an instance associated with bloody discharge from the foot. Guepin refers to a girl of eighteen who commenced to menstruate when three years old; at cessation of the menstrual flow she generally had a supplementary epistaxis, and once when this did not occur there was sudden effusion of blood into the anterior chamber of the eye. He also mentions hæmorrhage into the vitreous humor in a case of amenorrhœa.

Liebrich observed examples of retinal hæmorrhage in suppressed menstruation, and Sir James Paget saw a girl who had an effusion of blood into the anterior chamber of the eye at the menstrual epoch. Blair records a case of vicarious menstruation attended with conjunctivitis and opacity of the cornea, and Law speaks of a woman of thirty who bled freely from the eyes although menstruating regularly.

Instances of vicarious menstruation from the ear are mentioned by Spindler, Paullini, Alibert, Law, Barnes, Stepanoff, Field, Jouilleton and others. In Paullini's case there coexisted disease of the middle ear; in the case cited by Albert there was suppression of normal menstruation; in Law's case the menstrual discharge was suspended for several months; Jouilleton's example was a woman who menstruated from the right ear for five years following a miscarriage. Other instances reported are not dissimilar in any essential feature.

Hæmorrhage from the mouth, of a vicarious nature, has been frequently observed, the Ephemerides, Meibomius, Rhodius and others recording such instances. The case of Meibomius was an infant, the one mentioned by Rhodius was associated with hæmorrhage from the lungs, umbilicus, thigh, and a tooth cavity. Allport records a case in which there was recession of the gingival margins and alveolar processes, the consequence of amenorrhœa. Caso gives an instance of menstruation from the gums, and there is

record of a woman of thirty-two who had bleeding from the throat preceding menstruation. The menses ceased and the woman developed hæmorrhoids and hæmoptysis. Henry speaks of a woman who menstruated from the mouth, and Krishaber a case of lingual hæmorrhage at the menstrual epoch.

Pechlin cites an example of menstruation from the foot, Boerhaave from the skin of the hand, the Ephemerides from the knee, Albertus from the foot, Zacutus Lusitanus from the left thumb, Bartholinus from the hand, and the Ephemerides another case (during pregnancy) from the ankle.

Post speaks of a case of œdema of the arm alternating with the menstrual flow; Sennert mentions menstruation from the groin associated with hæmorrhage from the umbilicus and gums; Moses gives an example of hæmorrhage from the umbilicus, doubtless vicarious menstruation; Verduc details the history of two cases of menstruation from the scalp, and Kerckring cites three similar instances, one of which was associated with hæmorrhage from the hand.

Calder gives an account of menstruation at an ankle ulcer, and Brinckton has seen periodic bleeding from the cicatrix of a leprous ulcer. Hogg describes a young lady who injured her leg; the wound healed normally, but always "burst out afresh" the day preceding her regular menstrual period. Forster speaks of a menstrual ulcer of the face, and Moses two of the head.[3] White cites an instance of vicarious hæmorrhage from five deep fissures of the lips in a girl of fourteen.

Knaggs claims that as the sequel to an operation for ovarian disease there was a regular, painless menstruation every month, at which time the lower part of the wound reopened and discharged blood during the three days the catamenia persisted. McGraw has seen vicarious menstruation from an ovariotomy scar, and Hooper mentions an instance in which the vicarious function was performed by a sloughing ulcer. Depuytren speaks of denudation of the skin caused by a deep burn with subsequent development of vicarious catamenia from the site of the injury.

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[3] These cases may be duplicates. See those accredited to Verduc and Kerckring. Q. W. H.

Cases are recorded where vicarious menstruation took place from the rectum and urinary tract: Barbee saw a case in which cholera morbus occurred monthly in lieu of the regular menstrual discharge, and Barrett has noted vicarious menstruation from the rectum. Astbury observed the menstrual flow from hæmorrhoidal vessels. Rosenbladt gives an instance of menstruation from the bladder, and Salmuth saw a pregnant woman who also had a monthly flow from the urinary tract. Ford reports the case of a woman of thirty-two, the subject of a floating kidney, who began normal menstruation at fourteen and for quite a period had vicarious hæmorrhage from the urinary tract.

Tarnier mentions a girl without a uterus in whom menstruation proceeded from the vagina, and Zacutus Lusitanus relates a case of uterine occlusion with menstruation from the lips of the cervix. There is also mentioned a case where menstruation took place from the labia. In this connection menstruation after removal of the uterus or ovaries has not infrequently been noted. Storer, Clay, Tait, and others report cases in which menstruation took place with neither uterus nor ovary. Marsi, of Bologna, mentions the case of a young woman who had undergone radical vaginal operation for bilateral disease of the uterine adnexæ, it is presumed including hysterectomy. She menstruated from the bladder every twenty-eight days thereafter. At other times the urine contained no blood. She did not complain of any pain; see references, no. 2.

Vicarious or compensatory menstruation in the form of hæmatemesis, epistaxis and hæmotysis occurs with considerable frequency and numerous instances of this kind are on record; see references, no. 1.

Edson reports the case of a girl twelve years of age who had never menstruated in the regular way, but each month there appeared a bloody discharge from the nipples, quite considerable in amount, thoroughly saturating the clothing. It was pink in color and rather watery in appearance like the menstrual discharge of an anæmic or chlorotic girl. It contained blood corpuscles but no fat globules. The patient, however, was robust and healthy, but the breasts were not so large as would be expected in a girl of her age and physical development; see references, no. 3.

At a meeting of the Société Medicales des Hôpitaux de Paris

Lermoyez presented a girl aged sixteen years who for three years had menstruated from the right ear. The discharge was of non-coagulable blood and had a peculiar odor; see references, no. 4.

Hancock reports the case of a woman thirty-one years of age who had a discharge from the left breast which invariably began three days before the onset of the menses. It was at first whitish, then became sanguineous, and finally yellowish. It terminated suddenly when the menstrual flow appeared, but returned when the latter ceased, to last two or three days longer. This discharge first appeared one and a half years after the patient's youngest child was born, at which time the uterine cervix was lacerated, which latter gave rise to menorrhagia with scanty flow. The discharge from the breast had been a constant feature of menstruation since the foregoing occurrence. Other noticeable features were that the right breast always remained passive; galactorrhœa was present during nursing periods; and an escape of fluid occurred from the left breast during coitus [4]; see references, no. 5.

Weidner refers to a colored woman who had typical vicarious menstruation through the lungs or bronchial pasages, which occurred regularly every twenty-eight days, lasting three to four days. She had never menstruated normally; her vagina was apparently normal, the uterus undeveloped about the thickness of a finger and one and a half inches in length "running transversely across the roof of the vagina." Examination did not reveal the presence of ovaries, at least none could be felt. The woman was otherwise normally developed; see references, no. 6.

Irwin in recording three instances of vicarious menstruation occurring in women normally developed in all particulars, stated that he could not recall a single case of this kind where the subject was not fully developed both as to sexual organs and mammæ. One was a woman weighing one hundred and seventy pounds who every

[4] The editor of the Medical Age comments on this case in the following language: Vicarious discharge from the breast, which would seem to be more apt to take place than some other phases of vicarious menstruation because of the intimate connection between the mammæ and the uterus, is nevertheless of extremely rare occurrence; and it is open to some doubt whether this case is *de facto* one of vicarious menstruation. The case is recorded, however, as one of vicarious menstruation. Q. W. H.

three months had vicarious hæmorrhage; she vomited blood, and had profuse rectal hæmorrhage. There was no disease of the rectum to account for the hæmorrhage. It occurred regularly when menstruation should have taken place, one to three pints of blood being discharged each time. Another was also vicarious hæmorrhage from the rectum, less extensive, occurring once every two, three or four months, coming on gradually and lasting a day or two. The third case was vicarious hæmorrhage from the inner canthus of both eyes which occurred every twenty-eight days, and had persisted for sixteen years; see references, no. 7.

Barnett describes the case of a woman of thirty-three who was anæmic and poorly developed. At the age of thirteen she had "cramps in the uterine region from which it took her six months to recover." Later she suffered monthly pelvic pain, and one day during a paroxysm her nose bled profusely, and after losing considerable blood the pain subsided. Vicarious menstruation continued thereafter until operation was performed. Investigation showed a vulva normal in appearance, except that the clitoris was enlarged and there was no hymen. The vagina was one and a half inches in depth and small in calibre. There was detected in the pelvis a membraneous body which appeared to be a rudimentary uterus. The right Fallopian tube was enlarged to three times the normal size, the right ovary could be distinctly felt, but the left tube and ovary could not be found. Incision through the vaginal septum liberated a quantity of dark menstrual fluid. The vagina was enlarged and menstruation was established by the normal route on the fifteenth day after the operation; see references, no. 8.

Dolganoff records the case of a young woman with normal menstruation accompanied by the losing of blood from the external surface of the eyelids. The vicarious hæmorrhage appeared in minute drops like perspiration. The eyes were otherwise normal; see references, no. 9.

Rice refers to a woman who had typhoid fever following childbirth, and had not menstruated since the child was born. The sixth week she suffered pelvic pain and shortly thereafter hæmorrhage occurred from the mouth. It seemed to pour from between the teeth as well as from the roof of the buccal cavity. The administration of ergot aggravated the vicarious bleeding, and other drugs produced

no appreciable effect. The second day (having in mind vicarious menstruation) hot foot baths and hot vaginal douches were given, and the vicarious hæmorrhage ceased within an hour; see references, no. 10.

Buenting observed vicarious menstruation twice from the bronchi at a year's interval, and ten years later from the bladder, each time in the month of August. The young woman was in robust health with no symptoms referable to the organs involved; see references, no. 11.

Claiborne saw a girl aged sixteen who had hæmorrhage spots under each eye. She was pale, flabby and poorly nourished, but in other respects appeared well. First menstruation occurred at thirteen. Two or three days before each period a red spot appeared under each eye, from which blood finally oozed and formed a clot which dried, resulting in a "crust." This persisted during the menstrual period, disappearing gradually thereafter, the skin then becoming normal. Under tonic treatment her general health improved, but the peculiar phenomena mentioned were not influenced. The spots were semilunar in shape, about three-quarters of an inch below the level of the inner canthus and one-third the length of the lower lid. McAuliffe referred to a similar case in a review on ophthalmology published in *The Critic,* but gave no details. No record of any other such instances can be found; see references, no. 12.

Hiuzinga records an instance of vicarious retinal hæmorrhage in a girl of seventeen who had never been seriously ill, and who gave no history of specific or hereditary disease. Menstruation which began at the age of fourteen had been irregular the last year and a half and accompanied by slight disagreeable symptoms. During one period, while stooping to fasten her shoe, she suddenly became faint and dizzy. Everything seemed distorted and vision gradually became indistinct. Apparently the left eye was first affected, and later the right. Examination of the fundus revealed hæmorrhagic retinitis with numerous blood spots scattered over the field. The optic disc was slightly inflamed with borders indistinct, and there were a few blood clots in the vitreous. The external appearance of the eyes was that of ordinary conjunctivitis. Tight cold compresses were applied to the eyes and the patient

instructed to take a warm sitz bath three times a day. Artificial leeches were applied to the temples and two ounces of blood removed from each side. Potassium bromide and permanganate were administered internally, free catharsis was established, and menstruation passed without further trouble. The conjunctival congestion diminished, the vitreous cleared, the larger hæmorrhagic spots in the retina changed (becoming atrophic) and others disappeared leaving not a trace; but before this transformation was complete the next menstrual period arrived, and with it a repetition of the previous phenomena. Similar treatment again employed was followed by another (and last) retinal hæmorrhage the subsequent month; see references, no. 13.

That the views of the writers concerning the subject presented be not completely misunderstood, and in connection with their criticism of the statement accredited to Mr. Bland Sutton, it may be permissible to conclude:

*First.* That the definition of "vicarious" menstruation as given by latest medical lexicographers is recognized as only partially correct, but for the present is accepted;

*Second.* That the term is intended to represent a flow of blood (or similar fluid) from some other part than the vagina, and seemingly due to the normal menstrual tendency being misdirected;

*Third.* That in atypical cases the vicarious hæmorrhage may occur in connection with, or at the time of, regular menstruation, but from some other organ or part than the vagina;

*Fourth.* That in typical cases, the menstrual tendency (so-called) being completely misdirected, vicarious hæmorrhage takes the place of normal menstruation, the latter (*a*) never having been established, or (*b*) being entirely suppressed;

*Fifth.* That in some instances the vicarious hæmorrhage is to be regarded as distinctly compensatory in its significance, whereas in others it is but an accidental concomitant of normal menstruation;

*Sixth.* That it requires but superficial investigation to prove that not all cases recorded as vicarious menstruation are entitled to be so classified, that diagnostic errors not infrequently occur, and that medical statistics are not altogether trustworthy;

*Seventh.* It is believed, however, that sufficient evidence has

been presented to substantiate clearly the statement that vicarious menstruation is not a misnomer, and that Mr. Bland Sutton is entirely in error as to its being an "exploded superstition."

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# Genito-Urinary Diseases

## OPERATION: CONSERVATIVE PERINEAL PROSTATECTOMY FOR CHRONIC PROSTATITIS *

BY HUGH H. YOUNG, M.D.
Baltimore, Md.

GENTLEMEN: The patient whom I have selected for operation before you is one who has chronic prostatitis and not prostatic hypertrophy. I have selected this case because I think the subject of the operative treatment of chronic prostatitis is one of more interest at present than that of prostatic hypertrophy, about which so much has been written. In a recent study of 358 cases of chronic prostatitis [1] we found 34 cases in which definite obstruction to the free evacuation of urine was present in varying degree. In some cases there was only a slight bar, very little residual urine, the principal lesion being a contracture of the bladder produced by the muscular hypertrophy brought on by the increased difficulty of urination.

In four cases the residual urine varied from 65 to 150 c.c. In one case it was 440 c.c., and in two cases complete retention of urine was present and the patients led catheter lives. Since the publication of this article two additional cases of complete retention of urine and catheter life of long-standing, due entirely to chronic prostatitis in young men, have been encountered. There have also been a number of cases in which no obstruction to urination was present, but the pathological process was so severe and so rebellious to the ordinary methods of treatment, that it was thought wise to make use of operative treatment for a more radical removal of the chronic inflammatory tissue. In six such cases

* Remarks made before the Southern Surg. and Gyn. Assoc., Dec., 1906.

[1] "Studies in Urological Surgery," Johns Hopkins Hospital Reports, vols. 13 and 14.

the operation of conservative perineal prostatectomy has been performed, and the results have been so gratifying that I am inclined to believe that time will show the great advantage of operative treatment for the more severe cases of chronic prostatitis, even though no obstruction to urination exists. For those cases associated with obstruction there can be no question as to the advisability of operative interference, as shown by the beautiful results which have been obtained in my cases.

Our patient to-day is a case of severe chronic prostatitis with median bar formation, and considerable obstruction to urination which has led to hypertrophy and contracture of the bladder. He has also suffered from severe hæmorrhages from the posterior urethra, which have continued up to the present time. The prostate is not hypertrophied, and will not be therefore nearly so satisfactory for the ocular demonstration of the operation of " conservative perineal prostatectomy " as would have been possible with a case of prostatic hypertrophy, while the markedly indurated fibrous condition of the prostatic lobes will make the operation much more difficult than if we were dealing with large, globular, easily enucleable lobes. At the same time I hope to be able to show you by this case the advantages of the operation which I employ in even the most difficult cases.

The operative technique is shown in the diagrams which hang upon the wall; these are the same diagrams that have appeared in the Transactions of this Society.[2] The proper position of the patient is of great importance. As you see, I make use of Dr. Halsted's perineal board by means of which it is possible to elevate the hips greatly, so that the perineum is almost parallel with the floor. After the inverted V skin incision has been made, the space on each side of the central tendon is opened by blunt dissection with the handle of scalpel and finger until the triangular ligament is reached. A bifid retractor, which I have lately devised, is now introduced, and is of great assistance in dividing the central tendon and recto-urethralis muscle close to but without injuring the bulb. As you see now, I have cut no important structures, and with the exception of the two insignificant median line muscles the rest of the exposure has been made by blunt dissection. In this case there

[2] Vol. 17, 1905.

is more cicatricial tissue than usual around the membranous urethra, the exposure of which is somewhat difficult; but by proceeding carefully I hope to expose it without injury to the rectum, which lies very closely at hand. As you see now, I have pushed back the rectum for a short distance, the membranous urethra with the sound distending it is exposed to view, and I shall make a longitudinal incision into it. You now see the sound shining through the urethrotomy wound, and I shall proceed to pick up the edges of the mucous membrane with artery forceps. It is very important to catch the mucous membrane, as most of the difficulty experienced in introducing the tractor comes from invagination of the mucous membrane due to the failure of the operator to secure well the whole urethral wall before attempting to introduce the tractor.

I have now secured both edges of the mucous membrane, and having withdrawn partially the sound, which is in the urethra, I shall pass another sound through the urethrotomy wound into the bladder. Having removed this, I now pass the prostatic tractor, closed, into the bladder, and immediately open it out. Traction is now made upon it, and you see how much closer the prostate is drawn down into the wound. It is really quite close to the skin, but the rectum still covers most of its posterior surface, and in freeing it very great care must be taken else we tear it. I am careful to work against the posterior surface of the prostate, by cutting a fibrous adhesion here, and using the handle of a scalpel to push back the rectum there, gradually uncovering the prostate and working the rectum backward. I am convinced that most rectal injuries are produced by pushing directly against the rectum rather than working along the posterior surface of the prostate. The use of the finger is particularly dangerous, as there is great temptation to go too fast, and it is no difficult matter to poke a hole into the rectum with the tip of the finger.

I have now freed the entire posterior surface of the prostate, and, inserting this broad, sharply bent retractor, have an excellent view not only of the prostate, but of the seminal vesicles above it. You see that the capsule is fairly smooth, but slightly irregular; the prostate feels hard, and the lobes will not be enucleable as in the case of benign hypertrophies.

The capsular incisions, which I am now making, are a little

more widely separated than in hypertrophy cases, as I am particularly anxious to take no risk of injuring the ejaculatory ducts. These incisions are made about 1½ cm. deep, and the block of tissue between them contains the urethra and the ejaculatory ducts. Probably the most constant thing about the prostate is the position of the ejaculatory ducts, which lie in a pouch of fascia, always immediately beneath the floor of the urethra, the position of which can always be determined by the shaft of the tractor. I have never cut into the ducts in making these capsular incisions. The statements which have been made by certain writers in regard to the possibility of locating the position of the ducts are absolutely incorrect. There is no danger whatever of accidentally destroying the ejaculatory ducts or of producing impotence unless the operation be very carelessly done.

With this blunt dissector or enucleator I shall proceed to separate the capsule and urethra from the lateral lobes. You see here that the capsule is quite thin, and strips easily from the outer surface of the lobes. The urethra is more adherent, but the depth of the primary incisions has done most of the work and the rest of the separation is not difficult, for the lobes are now free everywhere except anteriorly and next to the bladder. Curved scissors are usually necessary to divide the anterior adhesions, after which I introduce my finger and complete the separation of the lobes. I find the deeper portion very adherent at the vesical orifice, and it will be necessary to make use of the lobe forceps, and free the deepest adhesions with scissors. During this procedure I entrust the holding of the tractor to an assistant.

The lobes are now removed and are very little larger than those of a normal prostate. I know that I have left none of the tissue of the lateral lobes because, with my finger, I can easily feel the blade of the tractor with only thin mucous membrane intervening.

The cystoscope has showed a small median bar; this is evidently so fibrous and adherent that it will be impossible to deliver it by means of the tractor into one of the lateral cavities, as is usually possible in cases of prostatic hypertrophy. I could, however, easily excise it through one of the lateral cavities without injuring the ejaculatory ducts beneath it or removing any of the urethral mucous membrane, but in this case I am anxious to inspect

and treat the posterior urethra, from which blood has been coming, and on this account I shall now open the posterior urethra along the left lateral wall, which, of course, leaves the ejaculatory ducts.

I use this same incision to remove large calculi from the bladder after prostatectomy, and no difficulty is encountered in extracting a stone over two inches in diameter. Examination of the floor of the urethra shows an enlarged hæmorrhagic-looking veru montanum, and several ulcers are seen along the floor of the urethra. I am now excising the portion of this redundant veru montanum, and shall curette the ulcers. The median portion of the prostate is definitely thickened. I can grapple it with a forceps, and by means of the sharp periosteal elevators and scissors have no difficulty in removing it without the mucosa covering it, and without destroying the ejaculatory ducts beneath it. Having removed the tractor, I now introduce my finger into the bladder and find that the small portion of the median bar has slipped back into the bladder. I have no trouble, however, in grasping it with forceps and excising it. The vesical orifice is now large, but the sphincter is still to be felt around the finger. I can easily feel most of the bladder cavity; there are no stones present, no diverticula, no ulcers or tumor, and nothing to suggest tuberculosis.

I shall now insert these two large catheters, which, as you see, have been divided obliquely at their ends and sewed together so as to form a common point to facilitate their introduction. These are introduced through the perineum into the bladder, and the lateral cavities are packed each with a single strip of iodoform gauze. You see I have not attempted to sew up the divided lateral wall of the urethra, as experience has shown that it heals perfectly well. Before closing, I always insert my finger, which is now gloved, into the rectum, and examine the anterior wall of this viscus. This is a very important procedure. You see that the rectum has not been torn into, but that the separation of the normally approximated levator and muscles has left the anterior wall exposed. You see how thin it is, and how without the support which is normally given it by the levators it could easily be ruptured by straining at stool, and that if a gauze pack were placed against it here necrosis might easily result. Both of these can be prevented by simply drawing the two levators together by a single suture of catgut, as

I am now doing. You see now how this thick mass of muscular tissue has been drawn together in front of the rectum, thus restoring the male perineum. Before adopting this plan, I had several cases of rectal break-down, due, I believe, to necrosis. I have now used this single suture of catgut to approximate the levators in 140 consecutive cases, and have not had a single rectal fistula as a result. This one suture has entirely removed all danger of the only bad result which I feared after this operation.

I am now closing the skin by interrupted sutures of catgut, leaving a small opening in front for the escape of the tube and gauze drainage. The tubes are fastened at the anterior angle of the wound with a suture of heavy silk. The bladder is now irrigated through one tube and out the other with salt solution. There is very little hæmorrhage. On return to the ward this irrigation will be continued for several hours, until the fluid comes away entirely clear, and all danger of the tubes becoming blocked by clots is removed. Using a two-gallon tank, very little difficulty is experienced in keeping up this irrigation, the inlet tube being clamped off so that only a small stream of fluid is allowed to enter, unless the hæmorrhage be profuse. The patient is generally given an infusion either on the table or after return to the ward. The gauze pack will be removed to-morrow morning, and the tubes in the afternoon. We generally have the patient in a wheel-chair on the second or third day, and instruct him to walk as soon as possible. He will remain in the hospital about three weeks, though some cases leave earlier. As a rule, the fistula closes during the second or third week. In several cases no urine has escaped through the perineum after the first week. There is practically no danger of a persisting perineal fistula. Sometimes, when the patient is very feeble or the bacterial urinary infection very severe, the closure may be slow, but if it is occasionally curetted (a gimlet curette has been found very satisfactory), and cauterized with nitrate of silver, the fistula always heals. Even while still present only a few drops of urine escape during urination, and cause the patient very little discomfort. No sounds are ever passed after the operation, as it has been shown that we have no stricture to fear. We usually pass a silver catheter before the patient leaves the hospital, so as to demonstrate that no residual urine is present.

In the operation which you have just seen, the prostate has been exposed almost entirely by blunt dissection, only two insignificant median line structures having been divided. The retraction of the levator muscles has been sufficient to expose thoroughly the field of operation. This is sufficient for the removal of very large hypertrophied prostates or for excising a carcinomatous prostate in its entirety with the seminal vesicles and neck of the bladder, as has been carried out by me in six cases.[3] The advantages of this technique are that no important muscle, sphincteric or sexual structures are destroyed; that the triangular ligament and its sphincter and the bulb overlying it are left intact, incontinence of urine thereby being avoided. The preservation of the urethra and the use of only a small linear urethrotomy in the membranous urethra back of the sphincter remove all fear of stricture. With proper retractors an excellent view is obtained, so that you see what you are doing, and the prostatic tractor allows you to draw down at will any portion of the prostate, and remove it without any of the mucous membrane covering it, and without injury to the ejaculatory ducts; none of which procedures are possible with suprapubic prostatectomy or a median-lined perineal prostatectomy done in the dark.

We have followed our cases very carefully, and have demonstrated that the operation, if properly performed, is always curative of the obstruction to urination; that it does not affect the sexual powers, and in fact in some cases in which the sexual powers are weakened or absent furnishes a restoration to normal vigor. This is probably explained by the removal of pressure upon the ejaculatory ducts and veru montanum. The mortality is *nil*. During the past three years the mortality rate has rapidly decreased, and in the last 110 cases there have been but 2 deaths, the last 68 cases being without a single death, every patient leaving the hospital well.

The remarkably good results which have been obtained in hypertrophy cases has led me to employ it more and more in cases of rebellious prostatitis with or without obstruction to urination, and I have now had about a dozen cases with excellent results. The sexual function, which is very important in these cases, has not been

[3] See complete report, Johns Hopkins Hospital Reports, vol. 14, and Southern Surgical and Gynecological Association Transactions, vol. 18.

impaired, and the discomfort which was caused by the persistent prostatitis has been removed.

I therefore believe that the perineal route is by far the most satisfactory for all forms of prostatic surgery, whether the condition is chronic prostatitis, prostatic hypertrophy or cancer, the great advantage being that you see what you are doing, that the exact nature of the disease can be determined, and the appropriate operation performed, and that in benign cases no important structures are destroyed.

# THE ETIOLOGY AND EXPERIMENTAL STUDY OF SYPHILIS

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Nothing justifies more clearly animal experimentation as a means of understanding and preventing disease in man, than the recent study of syphilis in apes. The end is not yet, but the last few years have taught us the cause of syphilis, and have encouraged us as to the ultimate suppression of this multiform and dangerous malady. It may well be a boast of the medical profession that its morality does not interfere with its humanity, and that syphilis has been regarded by the right minded physician as a disease to be cured, not as a punishment to be endured, even by the transgressor of social law. When we consider the innocent who suffer through heredity or direct contagion, the need of preventing as far as possible this dread disease is evident.

It has frequently been stated that a knowledge of Syphilis is equivalent to a knowledge of Medicine, and when we consider the manifold manifestations of the disease the statement cannot be denied. Syphilography is a specialty of medicine as distinct as Dematology, or Pediatrics. When we attempt a conception of the mountain of literature which has accumulated concerning this disease during the centuries it has been recognized, we are rather surprised to find how unsatisfactory is our knowledge concerning certain important phases of its contagion, evolution, and relation to other diseases. These unfilled gaps in our knowledge are due to the unavoidable incompleteness of clinical observation, however accurate, when deprived of the complemental evidence of experiment.

Indeed ever since the evolution of the experimental idea of studying human diseases by transmitting them to animals, attempts have been made to produce syphilis in the lower animals. Nearly all vertebrates, ranging in class from amphibians to birds and

mammals, have been injected with human syphilitic products in the hope of producing the disease in these lower forms. Although it has been claimed in a few instances that lesions like the primary lesion of man, the chancre, were produced, no disease at all comparable to the well-known Pox was ever produced, until the injection of an ape by Klebs[1] in 1879; this animal showed a distinct papular eruption after the injection of fragments of the hard chancre from a syphilitic. Similar observations were later made by Martineau and Hamonic,[2] by Sperk,[3] and by Nicolle,[4] but the only conclusion which could be drawn from the results of these observers was that most monkeys are refractory to the inoculation of syphilitic products, although now and again an individual may show symptoms resembling the disease in man.

In December, 1903, Metchnikoff and Roux[5] published the first of a series of memoirs on the experimental study of syphilis in monkeys, which, in conjunction with the work of other investigators, have led to an enormous increase of knowledge of the conditions under which syphilis is produced and how it may be prevented.

In their first communication Metchnikoff and Roux bring out clearly that success or failure in transmitting syphilis from man to monkey rests largely on the species of monkey chosen for experimentation; they found that different varieties vary enormously, though consistently, in their susceptibility to the disease. As might have been expected from other biological studies, those monkeys nearest to man in the animal scale, the anthropoid apes, are the only ones which may be said to take the disease typically, and to present it clinically as it occurs in man. The French investigators found in experimenting with small monkeys, that of five known as the Bonnet macacque (Macacus sinicus) two only gave a reaction to syphilitic products, in the shape of indurated sores; one mandril (Cyanocephalus mormon) proved refractory. It was found, however, that the chimpanzee (Troglodytes niger and Tr. calvus) when inoculated with syphilitic virus not only develops a typical chancre, after a period of incubation, but, a month later shows mucous patches in the mouth, a papular rash on the body and enlarged lymph glands. Moreover, it was found that the scrapings from a primary lesion in one chimpanzee gave rise to a typical disease in a second animal of the same species.

These fundamental observations of Roux and Metchnikoff were soon confirmed and amplified by other observers. Lassar [6] was able to repeat the results of the French investigators in chimpanzees and noted that the primary lesions correspond to the chancre of man histologically. Neisser,[7] who led an expedition to Java for the purpose of studying syphilis in apes, found that the gibbon and the ourang-outang were not so favorable as the chimpanzee for experimental syphilis. This observer in his first communication was not so successful in producing even primary lesions in the lower monkeys owing to certain imperfections of technique which have been improved by later observers.

Salmon [8] soon demonstrated that if macacus monkeys are inoculated on the cornea with syphilitic products, they will invariably react with a chancre. Thibierge and Ravaut [9] also obtained constant positive results by injection on the eyelid of these animals. Finger and Landsteiner[10] obtained 87 per cent. of positive results in lower monkeys by injecting a large amount of the virus. The consensus of opinions now is, that the chimpanzee is the animal of choice for the production of experimental syphilis; that it will invariably show a primary lesion and frequently secondary manifestations; the macacus or some of the other lower monkeys will usually give a primary reaction to syphilitic products if injected on the eyelid or cornea, but show no secondaries. In concluding the account of this initial phase of the study of experimental syphilis in animals it is well to mention the observations of Bertarelli [11] which have since been amply confirmed by Scherber [12] and Greef and Clausen.[13] Bertarelli noted that the injection of syphilitic products in the cornea of the rabbit gave rise frequently to a nodular growth of diagnostic value in the determination of syphilis.

In view of the successful prevention of rabies inaugurated by Pasteur, independant of any knowledge of the undoubted organism which is the cause of this disease, the prevention of syphilis, once its transmission to animals for the purpose of study was assured, might reasonably have been foreseen. But in the case of syphilis science has been more fortunate in determining the specific agent of the disease relatively early in its study. The announcement by Schaudinn and Hoffmann [14] early in 1905 of the constant occurrence in the scrapings from syphilitic lesions of a definite spiral

organism, the *spirocheta pallida,* was not only of astounding interest in itself but of great value in the study of the experimental disease.

The casual relation of certain accidental organisms in syphilitic lesions had been claimed by Lustgarten and others, but no one of these adventitious bacteria described has stood the test of corroboration and experiment. The exact nature of the Treponema pallida (Schaudinn) or Spirocheta pallida is still in dispute; it is doubtful whether it belongs to the bacteria or plant forms, or the protozoa or animal parasites. Concerning its causal relation to syphilis no doubt remains. Schaudinn and Hoffmann found the organism in the depth of primary lesions, in secondary papules and in the lymph glands of syphilitics; its presence was never noted in the lesions of other diseases; in certain ulcerated or complicated syphilitic lesions another spirochete, easily distinguishable by its refractility, the Spirocheta refringens, was sometimes found. The Spirocheta pallida is a very delicate spiral organism, detectable only with the highest powers of the microscope, and stained with difficulty.

The organism had been seen nearly two years before by Bordet and Gengou in syphilitic lesions, poorly stained by the ordinary dyes used for bacteria, but an extended search for it was abandoned by these authors when Metchnikoff was unable at that time to corroborate their findings in his syphilitic apes. The spirochete is 4-14 microns in length and at most only one-quarter of a micron in breadth; its form is that of a corkscrew with from 6 to 14 or even 24 turns. It is in active motion when examined in the fresh, and may show this activity for days in salt solution, when the tissues are kept at 20°–27° centigrade (Beer). It is well stained by a modification of the Giemsa stain proposed by its discoverers, although numerous other stains and modifications have since been suggested by other investigators.

Reference has been made as to the doubt which exists as to the proper classification of the Spirocheta pallida. Schaudinn classified it at first as a spirochete with the understanding that his classification of spirochetes as belonging to the Protozoa would be accepted. He regarded spirochetes, which had formerly been supposed to belong to the bacteria, as simply one phase in

the evolution of a protozoan organism of which another phase is the Trypanosome; that is, an organism showing a cycle of development. The more recent work of Schaudinn convinced him that the agent of syphilis could not properly be classified with other spirochetes which he had studied, and he later classed it among the bacteria under the name of Spironema (Vuillemim) or Treponema. This simpler nature of the Treponema pallida as an organism of a single form without a cycle has been the conception more generally accepted. Krzysztalowicz and Siedlecki,[15] however, claim to have found definite trypanasome forms in the organism and would class it as a protozoan.*

All attempts to grow the Spirocheta pallida have failed although a certain increase of the organisms in a mass of excised tissue has been said to occur in a few instances. Levaditi [16] succeeded in growing the Spr. refringens, which, it will be remembered, is sometimes a secondary invader in syphilis, in collodion sacs in the peritoneal cavity of rabbits.

We have accepted as proved, for the sake of exposition, that the spirochæta pallida is in reality the etiological factor in syphilis. Having considered the organism itself somewhat in detail, it is well to review the instances which have overwhelmingly demonstrated the causal relation of the organism to the disease.

In the few months following the discovery of Schaudinn and Hoffmann dozens of observers in all parts of the world were able to verify their observations; the organisms were everywhere found in practically all primary and secondary lesions of syphilis. They were found by Metchnikoff and Roux in the syphilis of apes. The spirochete was soon found by Buschke and Fischer [17] and by Levaditi [18] in the liver and spleen of congenital syphilis and later in nearly all the organs of still born syphilitic infants. Bertarelli Volpino and Bovero [19] found that the organisms could be stained in sections from the organs of hereditary syphilis by impregnation

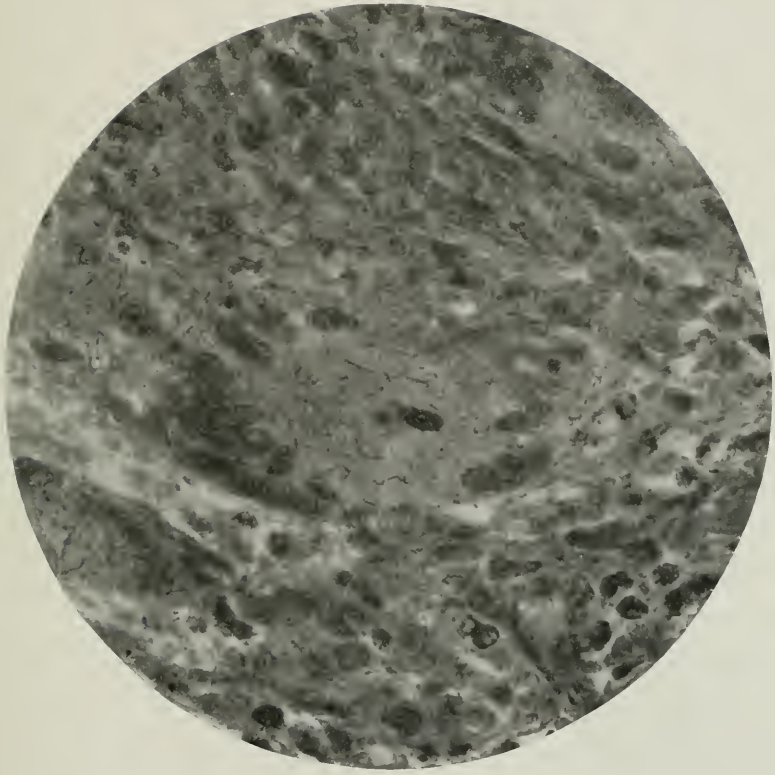
* The impetus which the discovery of the spirocheta pallida as the cause of syphilis has given to the study of organisms resembling it, which occur in other diseases, is enormous. Thus Castellani found a spirochete in the tropical disease, Yaws, the spirocheta pertenuis, which has been pretty generally accepted as the cause of this malady. The spirochete, originally described by Borrel, as occurring in spontaneous cancers of mice has lately been studied with interest by Gaylord and others in this country.

with silver nitrate, and Levaditi [20] enlarged their observations and improved the technique of staining. For a considerable time the presence of spirochetes in the blood of secondary syphilis was denied, but their presence was demonstrated indirectly by Hoffmann [21] who produced a chancre in a macacus monkey by injecting such blood; later the organisms were found in the blood by Raubitschek [22] and by Flugel.[23] In a similar manner it was proved that gummata are infective by Neisser [24] and by Buschke and Fischer,[25] and although the organisms in such lesions are very few in number they were finally found in the lesions by Doutrelepont and Grouven [26] and by Tomaszewski.[27] The interest of this latter finding in view of the supposedly non-infectious nature of tertiary lesions is considerable. Nattan-Larrier and Bergeron [28] found the spirochete in the placenta of a case of hereditary syphilis, and the organisms have been found in the ovary by Magahaes and Simmons [29] and in the Graafian follicles by Levaditi and Sauvage.[30]

As an idea of the regularity with which the organism may be found in the disease, and as further proof of its specificity, it may be mentioned that Mulzer [31] found it in 20 out of 22 cases of syphilis, but found no organisms in 56 cases of skin disease other than syphilis. Siebert [32] studied 73 cases of undoubted syphilis, 6 doubtful cases, and 46 cases of skin disease which were certainly not syphilis; among the 73 positive cases there were seven to be classed as tertiary and in these he did not find the spirochete; of the remaining 66 cases the spirochete was found in 52. The 46 controls showed the spirocheta pallida in no instance. Roscher [33] found the organism in 96 out of a hundred cases of syphilis.

The conclusion to be drawn from the literature, of which I have merely given the outline, is that the spirocheta pallida is the undoubted cause of syphilis since it has been found by observers in all parts of the world, in primary, secondary and even tertiary lesions of the disease, and in this disease only. Its occurrence in the blood of secondary syphilitics is of peculiar etiological significance. The spirocheta pallida is regularly to be found in the early stages of the disease, its demonstration depending on the skill and persistence of the observer. Moreover its appearance in the disease may be very early, and its presence may lead to the diagnosis of doubtful cases before the secondary lesions occur.

Fig. 1.



Section from human chancre by the Levadite method and showing the spirochæta pallida.
× 1000 diameters.

It has been demonstrated that syphilis can be transmitted to apes and that the anthropoid apes not only have the primary lesion but frequently show secondary symptoms. In the lower monkeys, a chancre may be induced by inoculation of the cornea, eye-lid or eye-brow, but in these animals no secondaries follow. In all these instances of experimental syphilis in monkeys the lesions show histologically the same structure as the corresponding lesion in man, and also show the presence of the specific spirochete when stained in the proper manner. It now remains to consider what results have been gained from the study of syphilis in apes that are of service in perfecting our knowledge of the disease in man, and more particularly as tending toward a means of prevention and cure of the disease.

It was found in inoculating monkeys with syphilitic products that uniform results could be obtained only when the inoculation is made in the skin by means of rather deep scarification or by making actual pockets in the epidermis. Subcutaneous, intraperitoneal and intravascular inoculation produce no results. This points clearly to the fact that the spirochete must propagate itself in the epidermis before a general infection, or even a local lesion can occur. It is found, indeed, in a histological study of the human or experimental syphilis that the spirochetes occur in numbers only in the lesions themselves and not in the organs or blood. The spirochetes are found grouped about the fine blood vessels in the chancre, or in the secondary papule, and they only slowly invade the blood vessel and then only to be carried to some distant point where, in a small vessel they increase in numbers, often forming veritable thrombi. They do not give rise to a general infection by multiplication in the blood stream except, perhaps, in the case of congenital infections where they occur throughout the organs and in the cell protoplasm.

This localization of the spirochetes primarily in the lesions themselves explains why a chancre, or papule, or lymph gland of man give the best virus for producing the disease experimentally. Mention has already been made of the difficulty of demonstrating the spirochete in the blood of syphilitics, owing, as we now see to their infrequent occurrence outside the specific lesions. When syphilis is transmitted from one ape to another, an idea can be

gained as to the relative amount of virus present in different organs; as in the transmission from man to monkey the secondary papules, mucous patches and glands are found the best means of transmission. The organs of a syphilitic ape rarely give the disease to another ape with the exception of the spleen, bone marrow, and testicle; the latter transmission is of interest in view of the hereditary transmission of the disease.

A careful study of the incubation period in chimpanzees shows that the usual time between the infection and the chancre is thirty days; the time between the chancre and secondaries varies from nineteen to sixty-one days. It is of interest to note that in the case of macacus monkeys, which it will be remembered show no secondaries and therefore are more resistant to the disease, the period of incubation before the primary sore is on the average one week less than in the more susceptible chimpanzee; the severity of the disease varies directly with the slowness of evolution.

It has been a pretty generally accepted theory that syphilis produces an active immunity in human beings; that is, an individual who has once had the disease does not contract it again. It was found in monkeys that two weeks after they were inoculated with virus, a second inoculation gave rise to no lesion, although the first inoculation went on to the characteristic lesion and secondaries; that is a local immunity occurs. It is therefore natural that from the beginning of their studies of experimental syphilis Metchnikoff and Roux should have aimed at finding some means of producing an active immunity in normal animals. In the case of diseases due to bacterial infection, immunity has been produced either by injecting cultures of diminished virulence (Pasteur) or killed cultures, or as in the case of diphtheria, by injecting the soluble toxines of the bacteria. It was found that syphilis virus when heated to 48° C. for one-half hour loses its power to produce lesions, but animals treated with such killed virus show no immunity on reinjection with virulent syphilitic products. When filtered through Chamberlain filters syphilis virus also loses its virulence but does not give rise to an immunity. Glycerine has no effect on the virus.

After many discouraging attempts Metchnikoff and Roux found that if a macacus rhesus was inoculated with human syphilitic

virus, and then the virus from this monkey transferred to another of the same species, and so on from one animal to another, the "virus of passage" took less and less time to produce a chancre. After fifteen or more passages the rhesus virus would produce a chancre in the rhesus monkey in seven days; that is, a fixed virus (virus fixe) was obtained, for further transmission did not lower the incubation period. If a chimpanzee is inoculated with this fixed rhesus virus it will show only a local reddening, and enlarged glands but no chancre and no secondaries; *such a treated animal, however, is found to be quite immune to virulent human virus.* This immunization by means of a fixed virus resembles the Pasteur method of treating rabies, but differs in that active immunity can be obtained by a single injection and not by repeated injections of increasing virulence.

By analogy the authors conclude that human beings can be vaccinated against syphilis, by inoculating them with a virus of passage from apes. The efficacy of such a treatment seems undoubted, but it is not quite so obvious as to whom such a treatment would be applied. Roux and Metchnikoff suggest that prostitutes might be assured by this method against the almost certain infection with syphilis which occurs to them in following their trade. It does not seem likely, however, that these unfortunates start on their career with their eyes open as to the dangers that beset them.

It is further pointed out that in certain districts of Russia practically all the peasant children are infected with syphilis by contamination from playmates who have the hereditary disease; here indeed seems to be a possible field for vaccination. That vaccination of human beings by means of a virus passed through apes does not in itself produce anything but the slightest lesions is attested for by two observations published by the eminent French scientists. One, a laboratory servant, who had handled the syphilitic apes, developed a slight swelling on the lip, which led to no further symptoms, but which showed the spirochetes and produced typical syphilis in a chimpanzee. Another man allowed himself to be inoculated with material from the syphilitic lesion of a monkey which had been transmitted through five animals from a human chancre; the volunteer showed only a few discrete indurated areas about the point of inoculation, and had remained perfectly well for

over a year at last observation. Neither of these individuals submitted to inoculation from a human chancre to prove their immunity.

Apart from the probability of a specific vaccination, Roux and Metchnikoff have experimented with medicinal means for aborting syphilis after infection. They found that when the area in monkeys which had been inoculated with virulent virus was rubbed vigorously with a calomel ointment,* even several hours after the infection, that the chancre was wholly aborted. Several instances have since occurred in human beings,[34] where the patient, two or three hours after sexual congress with a case of florid syphilis, has completely prevented the disease by use of this ointment.

All attempts hitherto to produce a specific serum in animals, curative for syphilis have signally failed. Dogs, horses and other animals have been injected frequently, with the blood of syphilitics in large amounts, but the sera of such animals show no effect on the course of the disease in human beings. People suffering from the disease have been treated by the injection of serum from those cured of syphilis but without effect. That the blood of men and apes, suffering from and recovered of syphilis contains specific bodies against the syphilitic virus has, however, recently been shown in an interesting manner. Bordet and Gengou introduced some years ago a method for determining the presence of specific antibodies in the serum of individuals which were immune to a given bacterium; it consisted in the fact that a mixture of the immune serum plus the causative organism forms a combination which fixes the alexine (complement), or normal ferment present in the blood. This " reaction of fixation " has been used by Wassermann, Neisser and Bruck [35] to show that the blood of syphilitic apes and men contains a substance (anti-body) which combines with the virus of syphilis. It has since been shown by several writers that the cerebro-spinal fluid of general paretics contains the same anti-body, a fact of great interest not only as a diagnostic means in general paralysis, but also as proving that general paralysis is in reality caused by syphilis.

As a result of the recent studies in syphilis of man and of apes

* Calomel 25 per cent., Lanolin 75 per cent.

we have learned: first, the cause of syphilis is the spirocheta pallida, an organism of which the class is as yet undetermined, and which has not been cultivated on artificial media; the spirochetes occur in the primary, secondary, and even the tertiary lesions of syphilis, and the infectiousness of these lesions varies directly with the numbers of organisms present. Secondly, we have seen that the length of the incubation period in animals varies directly with the intensity of the reaction to syphilitic virus; numerous details as to the contagion, distribution of lesions, and evolution of the disease have been obtained from the studies on syphilis in apes. Thirdly, it has been found that a fixed virus of passage in lower monkeys may be used to vaccinate higher monkeys against fully virulent human virus; and a similar treatment has been suggested as possible in man. In the mean time, as the result of experimental study, certain means of aborting syphilitic contagion have been suggested.

The production of a specific serum curative in syphilis is by no means improbable. The *sine qua non* for the production of such a serum is the successful cultivation of the spirochete on artificial culture media. The growing impression that even parasyphilitic affections, tabes, general paralysis, and the like, are due to the continued presence of the spirochetes as well as their toxins, renders some specific means of combating the organism highly desirable.

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# SPERMATIC INSUFFICIENCY AND DIASTEMATIC INSUFFICIENCY

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What are we to understand by testicular insufficiency? The answer to this question appears to be a simple one: It is the functional insufficiency of the male genital glands.

When we believed that the seminal gland was the only important portion of the testicle, the term "testicular insufficiency" was synonymous with insufficiency of the seminal glands; and this insufficiency occupied the same position as other forms of glandular insufficiency, such as that of the thyroid gland, for instance.

But nowadays we know that the testicle is composed of two separate and distinct glands that intertwine with each other: the seminal gland and the interstitial or diastematic gland (from diádryua, interstice, on account of its situation between the seminiferous tubes). The one of these two is contained in the seminal tubes; the second is situated in their interstices. They are relatively independent of each other, and their functions are altogether different.

Testicular insufficiency, when it occurs, does not necessarily concern both glands at once, but may, on the contrary, only affect one of them. It is therefore necessary to distinguish two chief forms of testicular insufficiency:

First. Insufficiency of the seminal gland, or spermatic insufficiency, that may go so far as aspermia.

Second. Insufficiency of the interstitial gland, or diastematic insufficiency, that may reach adiastematia.

This division of patients with testicular insufficiency into those with spermatic insufficiency and those with diastematic insufficiency is logical only if the functions of the two glands of the testicle are different, and, consequently, if the clinical signs caused by these two varieties of insufficiency are also different.

In previous publications we have shown that the interstitial gland is the gland of internal secretion of the testicle in mammiferæ.

It alone has the general effect on the system that was formerly attributed to the entire testicle. The sole function of the seminal gland is the elaboration of spermatozoa. These facts we have demonstrated by a quantity of cases and experiments which it is hardly necessary to recall here; we will merely refer to a few of the conclusions at which we arrived.

First. With certain cryptorchids the seminal gland is entirely lacking, while the interstitial gland has its full development. These cryptorchids are similar in every way to normal persons. (We have made two classes of cryptorchids: those similar to normal individuals, and those more or less like castrates. Those referred to above belong to the first variety.)

Second. When we effect experimental stenosis of the excretory passages of the sperm of animals (ligation of the vas deferens, or injection of zinc chloride into the epididymus), they remain like uncastrated subjects; in their testicles the seminal gland has undergone degeneration, while the interstitial gland has remained normal.

Pathological stenosis of the excretory passages of the sperm gives identical results.

Third. If with a young rabbit one testicle is removed and the vas deferens on the opposite side ligated, the seminal gland degenerates in the testicle that remains, while the interstitial gland undergoes compensatory hypertrophy that remains indefinitely. Animals operated on in this manner retain all the characteristics of uncastrated animals.

Fourth. When the development of the interstitial gland is stopped in young animals they present the exterior signs of castrated subjects.

These facts suffice to prove that the seminal gland has no general action on the system, and that this general action on the part of the testicle is due to the interstitial gland alone.

The functions of each of the two testicular glands being thus demonstrated, let us see what the signs are of the two varieties of testicular insufficiency referred to above; let us consider in succession the symptoms of spermatic insufficiency and of diastematic insufficiency.

Spermatic Insufficiency.—Let us take, for instance, a crypt-

orchid whose seminal gland has degenerated and whose interstitial gland has retained its normal development; or a man with whom pathological stenosis of the excretory passages of the sperm has occurred. The only symptom that such men present is that they cannot procreate. Their sexual desires and powers continue to exist, and are often heightened. Such a patient is normal from every other point of view, and nothing but microscopical examination of the sperm will enable you to diagnose the spermatic insufficiency. In the two instances mentioned there will be total insufficiency, or aspermia. Cases of less marked insufficiency are not so easy of diagnosis; still we must bear in mind that they do exist, and that spermatic insufficiency is normal in old men.

Diastematic Insufficiency.—Here the clinical aspect is altogether different, and varies with the degree of insufficiency, with the time of life at which it occurs, and with its duration. In certain cases the insufficiency is complete, that is to say that the diastematic secretion is entirely lacking; we shall call this condition adiastematia, and shall consider in rotation (*a*) early adiastematia, (*b*) late adiastematia, (*c*) diastematic insufficiency properly so called (and not attaining adiastematia); (*d*) temporary diastematic insufficiency.

*Early adiastematia.*—When adiastematia occurs at an early age, that is, if it manifests itself before puberty, the patient with whom it develops will resemble a man who has undergone castration.

Clinically the castrated individual is well known. He has no hair on either face or genitalia; his skin is white and soft to the touch; his face wrinkles at an early age; the penis is small and cannot enter into erection; the genitalia and annexed glands retain the infantile aspect; the breasts often develop; the patient's height is considerable, and the lower limbs are longer in proportion than is normal; the bony framework is slender and the pelvis wide, with the iliac portion opening outwards. Such a castrate has, in addition, a natural tendency to fleshiness, a complete absence of sexual desire, a characteristic tone of voice, and finally a generally indolent nature and frequent limitation of intelligence.

*Late adiastematia.*—When adiastematia appears later in life, after puberty,—as when caused by orchitis due to mumps or syphilis, or by a tumor of the testicle for instance,—the symptoms by

which it manifests itself are less striking than in cases of early adiastematia. The increase in stature, widening of the pelvis, as well as all manifestations of the bony system, disappear from the clinical tableau, if ossification is complete before the adiastematia appears; the beard and hair of the genitalia fall out in the majority of cases, the voice does not assume the same tone as in early adiastematia, but becomes hoarse, etc.; finally, certain signs may take greater predominance than others (the development of the breasts, or of the fat-tissue, for instance), whence possible varieties in the symptoms of late adiastematia.

*Diastematic Insufficiency properly so-called.*—When diastematic insufficiency falls short of adiastematia, the symptoms naturally vary with the degree of insufficiency and with the period of life at which it appears. The clinical tableau may therefore present in this case also a large number of variations and the diastematic insufficiency assume different forms.

A large number of cases described under the names of infantilism, gigantism, feminism, are to be grouped under this heading.

But the infantile, feminine or androgynous patients are cases where the insufficiency is very marked (differing from each other in all probability on account of the moment at which the insufficiency appeared, and also perhaps in its degree and duration); between them and the normal type of individual there is room for a whole series of these insufficient cases which must certainly exist but which have not yet been clearly recognized as such. Knowledge, however, of the adiastematic form, combined with minute clinical research, will no doubt enable these cases to be ultimately detected.

The study of these forms of insufficiency is much easier in animals, and we have noted a certain number among cryptorchid pigs. We have demonstrated that with some of these animals, intermediates between the boar and the pig, the varieties in size and weight of the interstitial gland (variations which correspond to those in the diastematic insufficiency) are accompanied by similar variations in the development of the genital tracts and of the annexed glands. Insufficiency in development of the genital tract is caused by the inadequate action of an interstitial gland with insufficient evolution. The seminal gland was lacking or only present in a rudimentary state with these cryptorchid animals; they were therefore all sterile.

But the interstitial gland may be insufficient even when there is a seminal gland elaborating spermatozoa. These cases of diastematic insufficiency will then be capable of reproduction, as opposed to the instances of spermatic insufficiency.

*Temporary Diastematic Insufficiency.*—There is a final factor that may complicate the clinical tableau of diastematic insufficiency: the duration of the insufficiency. For a state of transitory insufficiency is possible, and we have been able to bring it about experimentally in certain mammiferæ. In the case of a number of rabbits seven or eight weeks old we ligated the vas deferens. At the age of eight months a certain number of these animals showed with the greatest evidence all the morphological characteristics of infantilism and a complete absence of sexual desire. Microscopical examination of their testicles revealed that the seminal gland had remained in an embryonic condition and that the interstitial gland had not developed. Some of these rabbits were not sacrificed at eight months with the others, and at twelve months they showed noticeable transformation; their testicles had the same volume as those of adult animals that had not been ligated; the animals had acquired all of the anatomical characteristics of the non-operated animal and the genital instinct as well. Microscopical examination of the testicles then showed that the interstitial gland had attained its normal development and that the cells of which it consisted were voluminous and filled with secretion-products.

We had therefore been able to retard the period of puberty with these animals, which had only acquired the characteristics of the male at the age of twelve months, whereas these characteristics usually appear at the age of six months. In these instances the delay in the establishment of puberty is due to functional insufficiency of the interstitial gland, to temporary diastematic insufficiency.

If temporary diastematic insufficiency occurs in man, when will it show itself and how will it be revealed? Theoretically it may occur at all ages, but most probably it shows itself especially at the moment of puberty, the time when the interstitial gland must possess its maximum activity.

As for its clinical symptoms, they will necessarily vary also with the time of life at which the insufficiency appears; but they will be particularly evident before puberty and especially at the very stage

when puberty begins. These symptoms will be those that we see in adiastematic patients of that age, with the difference that they will be less pronounced and transitory.

In cases of young temporary adiastematia there will be manifestations of rapid and exaggerated growth of the limbs, delayed appearance of the beard, etc., retarded development of the external genitalia, late sexual desire, marked muscular apathy, asthenopia of accommodation, nervous debility, etc. Excess in growth is a sign that ought to be rarely lacking. In view of the marked action of the interstitial gland on the bones (as shown by comparative examination of castrates and cryptorchids of the first variety), it is logical to expect active stimulation of growth cartilages as a manifestation of diastematic insufficiency, whether transitory or not, appearing at the age of puberty.

It is well to mention also that this class of young patients is predisposed to tuberculosis, a fact that can be easily explained when we consider that the "invigoration" of testicular origin (or more accurately of diastematic origin) so thoroughly demonstrated by Brown-Séquard, is lacking in these patients.

We will not go more fully into the symptoms of diastematic insufficiency, as we are not in possession of the necessary materials for a thorough clinical study of this insufficiency. We simply desired to draw attention to the lack of precision in the term testicular insufficiency, and to show that it ought to be replaced by those of spermatic insufficiency and of diastematic insufficiency, which apply to entirely different clinical types.

# Ophthalmology

## A CONTRIBUTION TO THE STUDY OF OCULAR BIRTH INJURY

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The fact that the eyes of the child are subjected to considerable risk of injury during instrumental and other difficult labors is becoming more prominent as ophthalmic surgeons and obstetricians in various parts of the world, recognizing the importance of the subject, watch for and report new cases. Every year brings, from our own experience and from that of others, a widened view of the scope of the subject and it is with the object of interesting, not only those specially working at ophthalmic surgery and obstetrics, but also the general practitioner, that this paper is written. So far as we are aware, no case has yet occurred in which the question of an ophthalmic condition being due to accident at birth has been brought into the law-courts, but nevertheless there is abundant possibility that at some time it may be brought up, and on this account, we would draw the attention of the medical-jurist also to the subject.

The nature and variety of the injuries which may occur would require, for their complete description, more space than is here at our command and we shall, therefore, content ourselves with a brief recital, taking up in detail only a few points.

Ecchymosis of the eyelids, with or without actual breaking of the skin, is of frequent occurrence and is often accompanied by ecchymosis of the conjunctiva, protrusion of the eyeball and retinal

hæmorrhage. The proptosis which occurs in such cases varies greatly in amount and is probably due to collapsing of the orbit and consequent hæmorrhage behind the eye. In some cases the collapse of the orbit is so great as to cause extrusion of the eye and rupture of the optic nerve or ocular muscles. Retinal hæmorrhages are frequently seen after difficult deliveries and in the majority of cases cause no permanent defect, but probably some of the unexplained fundus changes seen in later life may be due to them. The cornea may be injured either by direct pressure or, probably more commonly, by increase of intraocular tension. The iris may be injured, a rupture of some of the bloodvessels taking place resulting in effusion of blood into the anterior chamber, or the iris tissue may be ruptured. Effusion of blood into the vitreous humor may take place from injury either to the ciliary body or to the retina. In cases where the pressure on the eye has been very great, extensive damage to the interior of the eye may take place, leading to total destruction of the organ. We have seen hæmorrhage into the optic nerve, and subchorioidal hæmorrhage following birth-injury, conditions which, had the child survived, would have led to serious defect of vision. Besides these purely ocular injuries it must be remembered that the visual apparatus may be seriously affected by hæmorrhage into the cranial cavity, either submeningeal or intra-cerebral and that, whilst nothing can be seen in the eye at an early date, late changes may develop which indicate that the visual functions have been interfered with (bilateral optic nerve atrophy and nystagmus). Again, the pressure brought to bear on the orbit may cause rupture of some of the ocular muscles and convergent or other strabismus may be present at such an early date as to indicate birth-injury as its cause.

As regards the precise mode of origin of such injuries there is room for considerable doubt, as it is not always that the exact position of the blades of the forceps used in assisting labor can be stated. It is undoubted that the great majority of injuries occur during assisted labor, but many occur also in the course of difficult unassisted births. Thus palpebral, conjunctival and retinal hæmorrhage have been seen, and not infrequently there is a certain degree of proptosis oculi.

Only in one such case of unassisted labor have we seen a corneal

lesion, and that not a permanent one. Whilst, then, the use of mechanical assistance is a determining cause of injury in most cases, it is not clear precisely how the lesions are produced. It is probable that either of two factors may be present, (*a*) the blades of the instrument may press directly upon the eyeball, or (*b*) the blades of the instrument may be applied to the head in such a position that the head is flattened either laterally or obliquely and the orbits collapsed more or less completely. As a result of this orbital collapse the eyeball with its contents is greatly pressed upon and a very high degree of interior tension is developed. Whilst this is so it is easy to see how the bloodvessels in the eye and lids may give way, causing ecchymosis; how the cornea may be stretched to such a degree that it ruptures posteriorly, or how the bony orbital wall may be fractured and spicules of bone be driven into the orbit and there cause damage to the nerves and muscles.

In the extreme case of the orbit being flattened to such a degree that the eye is extruded from its socket, either the muscles and optic nerve may be torn or cut through and the eye lie on the cheek practically free, or, the connections not being ruptured, the prominent eyeball may be, for a time, prevented from returning to its normal position by the occurrence of hæmorrhage into the orbital tissues when the pressure is released. Apart from the more or less direct agency of the forceps in causing such collapse of the orbit we are well aware of the fact that the pressure of the head on a marked sacral promontory in a rickety pelvis may, by causing a depression of the cranial vault, give rise to the same effect. Whilst formerly we considered that the majority of corneal injuries were the result of direct pressure it now becomes probable that the second mode of origin is more frequent.

We have already pointed out[2] that in Glasgow a larger number of cases of birth-injury is seen than in any other city with which we are acquainted because of the prevalence of rickets, and this we still hold is the case. Bruno Wolff[5] pointed out the fact that birth-injuries are more frequent where forceps are applied at the brim of the pelvis than when they are applied low, and this we can fully confirm. It is probable that the precise nature of the injury, given the same degree of pressure and resistence, will be determined, to some extent, by the exact position of the head with

regard to the bony prominences of the maternal passages. Thus we can understand that if the orbit is collapsed and the eye has room to stand out without pressing against any hard part, simple proptosis may occur, whilst, if the eye is thrust strongly against the bony wall, high interior tension will be developed and damage to the eye will result. It is in such cases that hæmorrhages into the eye may be seen and also that the posterior surface of the cornea may be ruptured.

From what we have said it is clear that such injuries to the eye cannot be absolutely prevented if the child is to be born without having recourse to the extreme of Cæsarian section. The pelvis is very narrow and, if the head is to be pressed or pulled through, great force *must* be used, and not even the most skilled accoucheur can say with precision in what position it is being applied. Hence, we would have it clearly understood that no blame can justly be laid on the obstetrician for the occurrence of such injuries. Since our clinical observations include a relatively large number of cases of corneal injury, not only in the recent condition as in the new-born, but also in the healed condition as seen in older children and in adults, we shall occupy some space in describing these injuries, and in detailing the pathological changes observed *post mortem*.

If after every difficult labor the eyes of the child are minutely inspected under a good illumination it will be found that in a certain small proportion of cases one or both corneæ present a more or less abnormal appearance. In the slightest cases—and we are sure these must occur all over the country—a faint uniform haze of the cornea is seen, associated with a certain amount of loss of polish of the surface. Magnification of the cornea reveals the fact that in its substance there are numbers of flocculent dots. There can be no doubt that this condition is due to œdema of the corneal spaces. If this opacity be uniform and if it be slight it will probably disappear within twenty-four hours or so, and leave no trace. It is doubtless due to this evanescence that such corneal œdema has not been more frequently noticed.

But, in a proportion of cases of difficult labor, a proportion not yet reducible to arithmetical terms, a more permanent injury results. It must be admitted that even this may pass unnoticed in the earlier weeks and may then become so difficult of detection through the

clearing up of the more apparent part of the opacity that it is entirely overlooked until later years when visual troubles lead the patient to the oculist; and the latter, even, if not on the *qui vive,* may fail to appreciate the true origin of what appears to him, on a casual observation, merely to be a case of high astigmatism.

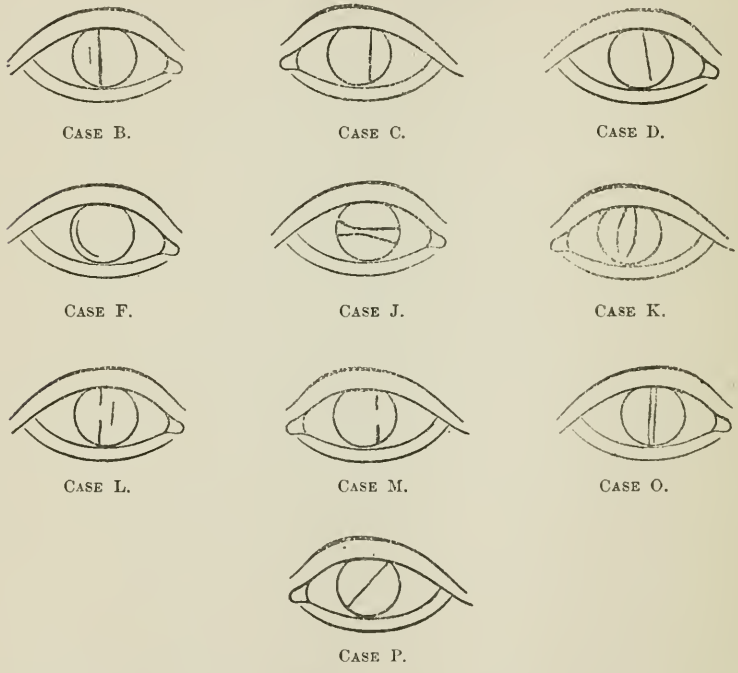
The appearances and course are somewhat as follows: In a newborn infant whose head has been subjected to very severe pressure,—by the promontory, by the forceps, by both combined, or even merely through a disproportion between the head and the pelvis, or the occupation of the passages by some other portion of the child in addition to the head—it may be found immediately or soon after birth that there is a corneal haze of considerable intensity, and a marked loss of surface polish. The most careful examination may reveal nothing but this uniform opacity, but, more often than not, the haze will be found to be not uniform but interrupted, as it were, by one or more bands or stripes which, at the earliest observation, may be very indefinite, giving one merely an impression that the refraction of the cornea is altered along the line of the stripes. A reference to the chart of the resulting linear opacities, (fig. 8,) will show that the direction taken by the striping is usually approximately vertical, and reference to the tables that in most cases there has been pressure on the orbit by a forcep's blade, or a diminution in the capacity of the cranium by a promontory-corneal depression.

Now, whether at birth only a considerable uniform opacity or an opacity with striping had been noticed, it nearly always happens that in a few hours or in a day or two the general opacity becomes much greater and obscures the view of the stripes if such existed. The cornea may become so opaque that the observer may think vision must be entirely lost. Yet, after a while, days, weeks or even months, this opacity lessens, and as it gradually disappears the stripes reappear or come into view for the first time if they had not originally been observed, and the corneal surface regains its polish. But the stripes have now taken on a different aspect. Whereas immediately after birth they seemed rather to be due to what may be called refractive opacity, they are now quite definitely narrow white lines such as are caused by scar tissue. As time goes on these lines become more sharply defined, though fainter and more difficult to detect except against the black background of a

dilated pupil, and eventually they may become so faint as to deserve rather the designation of a refractive opacity, which almost defies detection except by the aid of the ophthalmoscope mirror or focal illumination. What, then, are these lines? it may be asked. It may be stated positively that, in the early stage, they are evidences of the existence of ruptures of the posterior surface of the cornea, and that, in the later stages they are the results of cicatri-

CHART.—FIG. 8.

*Showing the positions of linear opacities in ten cases observed clinically. (Cases observed only pathologically are excluded.)*




zation of these ruptures. We have been able to make histological examinations of three cases in which lines were seen and in each case the posterior surface of the cornea was found to be lacerated.[2] It is interesting to note that, whilst we have not had an opportunity of examining histologically the cornea of any case in which repair had advanced to any notable extent, Peters of Rostock[6] had examined an eye twenty-four days after birth and his findings

amply corroborate ours, for he found a rupture in course of cicatrization.

Turning now to another, and, for practical purposes, a more important point in connection with the subject of corneal lesions it may be asked, What is the influence of these internal scars on vision in after life? This we are well able to answer, having seen now, at the clinic of the Glasgow Eye Infirmary, five cases in which scars indubitably the result of birth-injury were found on the posterior surface of the cornea. We have found in all these cases that the presence of these faint scars exercises a very bad influence on vision because of the high degree of astigmatism produced. This being so, it is of the greatest importance to be able to recognize the presence of such scars, and it may be stated at once that as the early presence of corneal changes requires careful investigation for its detection, later even greater care is necessary. The lines in later life are very easy to miss and only the most careful watching will enable one to detect their presence. In three of the cases which we have seen attention was drawn to the subject by the discovery of high astigmatism which was present in one eye only, and such unilateral high astigmatism should at once lead to a suspicion of birth-injury. It may be noted in examining a case of this kind that there is something which cannot be well defined, interfering with a distinct view of the fundus on ophthalmoscopic examination. Superficial examination will allow this to pass, perhaps as a nebula of the cornea, but if a plus 12 D. lens be put on behind the mirror and the cornea attentively observed in all directions and at different distances, it will be seen that the haze is not a diffuse one, but is composed of curved lines, not, as a rule, parallel, but enclosing a space shaped like a barrel-stave. They are faint, hair-like lines and the space enclosed is often finely dotted over with irregularities.

We have elsewhere stated that the lines are rather refraction opacities than true opacities, and on this account we recommend the use of focal illumination in a completely darkened room, by which means the detail of the lines may be seen more clearly than with the opthalmoscope. On examining such a case and finding the high astigmatism and the peculiar lines in one eye only, it is incumbent on the observer to inquire into the history of the birth. In two of our cases scars of cuts on the temple and occiput were pointed

out by the mother, indicating the position of the blades of the forceps; and in the two others the history bore that the child's face was black for a long time after birth.

The last case of this kind which we saw was that of a girl of nineteen years who came to the Infirmary complaining of dimness of vision of the right eye, and headaches. This case is of peculiar interest in several respects. The presence of the characteristic scars was recognized at the Out-door Department by one of us and inquiry brought out the fact that the child had been born after a prolonged and very difficult assisted labor conducted by one of our best obstetricians. The girl had long ago known that the vision of the eye was defective, but only three years before seeing us had she consulted anyone on the subject. The oculist consulted then recognized the high astigmatism and noted that there was a "nebula" of the cornea but did not see the lines. The obstetrician had noted that there was ecchymosis of the eyelids but nothing else. The vision amounted to fingers at four feet only and with the best correction, namely -9 sph. with -4 cy. ax. 75 was only fingers at 17 feet.

We have been able to satisfy ourselves by ophthalmometric examination that the astigmatism is entirely corneal in all cases and it varies in amount from four to ten dioptres. The astigmatism, in accordance with the position of the lines, which were nearly vertical in direction, was against the rule. From what has been said, then, it will be understood that the results of birth-injury to the cornea may be very serious so far as vision is concerned. Before leaving this part of the subject it must again be remarked that if at or soon after birth, no lines develop and only a haze is seen, then the whole opacity may clear away leaving no bad result. In other words it is the ruptures which do the damage and a simple haze, due to œdema of the cornea will clear up and leave no ulterior defect.

Turning our attention now to that group of cases in which ocular disturbance is brought about in consequence of damage done to the brain or its membranes, we have to notice that this is one of the most important classes. Here, not only the eyes but the general nervous system may be very severely affected and it is within our knowledge that the first sign of the existence of such damage may be seen in the eye. Not infrequently a child is

brought by the anxious mother to the Eye Clinic with the complaint that the child does not "take notice" and this we have found, in two instances at least, to be the case where the labor had been specially difficult. In one case the child, which had had several convulsive seizures after birth, was six months of age, had distinct lack of fixation, even bright lights failing to attract its attention. Ophthalmoscopic examination was very difficult, but it was ultimately found that there were no signs to indicate the existence of fundus change. The nerves were, perhaps, small but not pale and the vessels were of good size. It was noticed soon after this, by the mother first, that the child could not or did not turn the eyes to the right of the middle line, whereas they frequently deviated to the left. Later, the arms became rigid and the hands clenched and, although the limbs could be extended, they always returned to the primary position. The child did not make any attempt to crawl or move on its own account, but always took the breast well. Although it is now eighteen months of age there is no sign of improvement in the child in spite of various kinds of treatment, medicinal and electrical. The general nutrition is good but the intelligence is very poor, the child being probably imbecile. Wolff[5] gives an account of a case of somewhat similar nature in which the child died, apparently idiotic, at the age of three months. We have seen the results post-mortem, of severe injury to the head of an infant[2] where there had been severe hæmorrhage into the cranial cavity and the brain had been much injured, and argue from this that children whose brains have been injured may not all die, and that those who do survive will probably have lifelong defects of musculature and intelligence.

The question naturally comes up here, Could anything be done for such cases if they were recognized early enough? It is quite positive that the early evacuation of the bloodclot would relieve pressure and we think that the careful watching of suspicious cases and the observation of the results of autopsies on cases of still-born children would certainly lead to the discovery of much useful information. Short of such serious developments as above mentioned, however, it it highly probable that many cases of congenitally blind children are so as a result of birth-injury which has not been recognized, and it is to be desired that as many cases as possible of this

nature should be recorded and thus be available for reference. We know, for instance, of a case which occurred in the practice of a physician of this city and which has not been recorded although it is of great interest and importance. The child died at the age of eight months or so, apparently blind and imbecile, the birth having been an exceedingly difficult one.

We have the impression that if it were better recognized that damage done to the head of the child is not always avoidable, a greater number of such cases would be recorded, and therefore urge the point upon the notice of practitioners as highly important.

The last group of cases which we would take up for special notice is that in which the eyes are involved as the result of injuries to the orbit. Compression of the orbit as before noted is a highly important factor in connection with purely ocular injury, but besides this the various nerves and muscles in and near the orbit may be damaged by pressure or by the intrusion of a spicule of bone. So far as we are aware there are recorded about ten cases of complete extrusion of the eye from the orbit and in some of these the orbital wall was known to be fractured. In many of them there was a spoon-shaped depression of the cranial vault as evidence of the pressure exerted by the sacral promontory. In others, however, the pressure had been lateral and marks of forcep's blades were seen. In about twelve cases recorded the facial nerve has been injured by pressure.

Regarding paralysis of ocular muscles in connection with birth-injuries, a considerable number have been recorded, and we have lately seen an instance at the clinic of the Eye Infirmary. A boy of seven years of age came complaining of having a squint since birth and on inquiry it was found that the statement was actually true. The mother pointed to a scar on the temple which she averred had been produced by the pressure of the forceps during a difficult confinement. She further stated that the face had been black for some weeks after birth. The boy had very defective vision and nystagmus, but there was no evidence of the eye having been injured. The refraction was H plus 4 in each eye and correction of this error did not greatly improve the vision.

In concluding this paper we would remark on the fact that Wolff has collected 108 cases of birth-injury to the eye and its

annexes, our own included, down to the year 1904. To these we can add probably 20 (some of which remain to be published) seen during the last three years in this city, and there are, doubtless, several cases which have been recorded in other countries, so that in all there cannot be far short of 150 cases in literature, which are all that have been noticed during the fifty years or so that have elapsed since the subject was first drawn attention to by Pajot. Now it is a striking fact, in the face of this, that in one clinic at one Eye Infirmary at least eight cases have been seen which have occurred at dates, varying from nineteen years to one year previously and had been passed over at the time. Probably the future will show that many other cases are at present waiting discovery. Glasgow admittedly has hitherto shown a much greater number of cases than any other city, but this somewhat unenviable notoriety may not only show that more cases do occur, but that much more attention is given to the matter than is the case in other cities.

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[6] Peters,—Eine Verletzung der Hornhaut durch Zangen-entbindung mit anatomischem Befund. Arch. f. Augenheilk, 1906.

## TABULAR STATEMENT OF TWENTY-TWO CASES OF BIRTH INJURY OF THE EYE.

| Case and Reference. | Particulars of the Labor. | Corneal Lesions. | Cranial and Orbital Lesions. | Lesions of the Cerebrum, Conjunctiva, Retina, Nerves, Muscles, Eyelids, etc. | Particulars of the Child. | Remarks. |
|---|---|---|---|---|---|---|
| Case A..... Muir, aged 19. (Thomson and Buchanan, *Trans. Oph. Soc. U. K.*, 1902; *Ophthalmoscope*, 1905.) | Primipara. C. V. 3½ inches. Prolonged first and second stages; vertex P. "Very difficult delivery." Forceps at brim: (1) over outer angle of R. orbit; (2) not stated. | At birth, R., vertical stripes; L. general slight opacity. (See Figs. 1 and 2.) | None noted | R. A. C. full of blood. P.M. Blood on post-corneal surface. Ruptures of Descemet's membrane and layers of cornea. Retinal, choroidal, and optic nerve hæmorrhages. L., retinal hæmorrhages. | Stillborn. F. 7¾ lbs. | For full account of pathological findings see papers referred to in Column 1. |
| Case B ..... Kennedy, age? (Thomson, *Trans. Oph. Soc. U.K.*, 1902; Thomson and Buchanan *Ophthalmoscope*, 1905.) | ? Primipara. C. V. 3½ inches. Vertex P. (almost certainly). "Considerable difficulty" in delivery. Forceps at brim: (1) over right temple; (2) not stated. | 3rd day, R., general opacity; L., clear. Later, vertical stripes appeared in R. (See Fig. 7.) | None noted. | Ecchymoses conjunctivæ. | Living. M. 9¼ lbs. | Linear opacity quite visible at 20 months. |
| Case C ..... Crawford, age? (Thomson, and Thomson and Buchanan loc. cit.) | ? Primipara. C. V. 2¾ inches. Vertex P. (almost certainly). "Great difficulty" in delivery. Forceps (1) "Near R. eye;" (2) not stated. | At birth, R., great general opacity; L., slight ditto. 8 days later, R., intense general opacity; L., vertical stripe. | Spoon-shaped depression of L. frontal bone. Left eye proptosed. | Large clot in L. conjunctival sac. | Living. F. 7. lbs. | Case lost sight of. |

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| CASE D ..... M ..—, age? (Thomson, loc. cit.; Thomson and Buchanan, loc. cit.) | Marked sacral promontory. "Great difficulty in delivery." Forceps at brim: (1) over left temple; (2) over right ear and neck. Other details wanting. | Three weeks after birth, obliquely vertical stripe seen on left cornea. | None noted. | At birth, left eye was "contused and swollen;" conjunctival sac contained blood-clot. | Wanting. | This case was not seen by us till 6th week. Opacity of cornea confirmed. At 3½ years the linear opacity was still faintly visible. |
| CASE E ..... Name and age unknown. (Thomson and Buchanan, loc. cit.) | Craniotomy. | P.M. Rupture of Descemet's membrane of R. eye. (See Fig. 4.) L. eye destroyed. | ..... | Retroversion of lens and vitreous. For details, loc. cit. | ..... | This case is stated merely to show the possible results of great pressure. |
| CASE F ..... Percy, aged 38. (Thomson and Buchanan, *Trans. Oph. Soc.*, 1903; *Ophthalmoscope*, June, 1905) | Multipara. C. V. 3 inches. Stages 1 and 2, 18 hours. Forceps and symphysectomy after failure with forceps alone at brim: forceps almost ant. post. removed and reapplied in biparietal at outlet. | At birth, R. cornea hazy; became opaque and remained so for long time. Crescentic linear opacity eventually remained. Remainder of cornea cleared. L. eye extended. P. M. Rupture of Descemet's membrane and post corneal layers. (See Fig. 3.) | L. Fronto-parietal spoon-shaped depression 6 cm. x 4.5 cm. Accoucheur elevated same by fronto-occip. counter-pressure. Eye extended from L. orbit onto cheek, only held by conj. and ext. rectus. Orbit filled with clot. No laceration of lids. | L. conjunctiva, optic nerve, and orbital muscles cut or torn. Left eye. P.M. Slight retinal œdema, optic nerve cut or torn at 16 m.m. behind eyeball. | Living. F. 8½ lbs. Head measurements: BT., 3¼ inches; BP., 4¼; SOB., 4¾; OF., 4¾. | Combination of small pelvis and large head disastrous to left eye and causing severe corneal injury to right eye. Probable that a plate or spicule of bone divided L. ocular muscles and optic nerve, thus accounting for blood in orbit. Compare Case T. Child healthy at 17 months. |
| CASE Fa ..... Sloan, aged 28. (Thomson and Buchanan, *Trans. Oph. Soc. U. K.* 1903, Case 3.) | Multipara. C. V. 3 inches. 1st and 2d stages, 12 hours. Vertex P. "Very difficult delivery." Forceps at brim: (1) over right parietal region; (2) over left mastoid, left ear, and parietal region. | None. | Skull compressed laterally. Fissured fracture of lower outer part of left frontal bone ½ inch above orbital plate. | Ecchymosis conjunct. Clotted blood in R. ant. chamber. L. retina œdematous and slightly hæmorrhagic. Small intracranial hæmorrhages opposite points of application of forceps and other large hæmorrhages over other parts of cerebrum. | Stillborn. M. Well nourished, large child. Respiration could not be started, though heart beat for 5 minutes. | The intracranial hæmorrhages found post mortem and the fact that respiration could not be induced are the features of this case. |

TABULAR STATEMENT OF TWENTY-TWO CASES OF BIRTH INJURY OF THE EYE.—*Continued.*

| Case and Reference. | Particulars of the Labor. | Corneal Lesions. | Cranial and Orbital Lesions. | Lesions of the Cerebrum, Conjunctiva, Retina. Nerves, Muscles, Eyelids, etc. | Particulars of the Child. | Remarks. |
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| Case Fb ..... Name? (Thomson and Buchanan, *Trans. Oph. Soc. U. K.*, 1903 (Case 4).) | Details wanting. Forceps at brim: (1) over outer angle of R. orbit; (2) over ramus of left lower jaw. | P.M. Right eye, abrasion of ant. corneal epithelium; œdema of cornea. Post. epithelium stripped off. | Much head moulding. Extreme mobility of bones of cranial vault. Depression of ext. inf. angle of right frontal bone below the molar. | Small hæmorrhages over R. frontal convolutions and cribiform plate. Blood collections in left middle fossa, post. fossæ on tentorium cerebelli. Great ecchymosis conj. Blood in left A. C. Right retina œdematous and hæmorrhagic. | Stillborn. Sex? Very large child. | Do. |
| Case Fc ..... Hood, aged 34. (Thomson and Buchanan, *Trans. Oph. Soc. U. K.*, 1903 (Case 6).) | Multipara; 7 previous labors instrumental; 4 children stillborn. Pelvis contracted; 1st and 2nd stages, 8 hours. Vertex P. No notes as to position of forceps. | None. | Right eye proptosed at birth; returned to normal within 8 days. R. fronto-parietal spoon-shaped depression 4 cm. x 3.75 cm.; elevated within a few hours of birth by fronto-occipital pressure applied by accoucheur. | R. conjunctival ecchymosis; ecchymosisof lids; small retinal hæmorrhages. | Living F 7½ lbs. | The proptosis was doubtless due to retrobulbar hæmorrhage. The palpebral ecchymosis was not marked at first, but became extreme by 3d day. This is a case in which serious defect of vision might be expected to ensue; but case was lost sight of. |
| Case G ..... Burns, aged 31. (Thomson and Buchanan, *Ophthalmoscope*, 1905) | Multipara (10). Instruments once previously. Pelvis not cont. 2d stage, 13 hours. Presentation of face, arm, and cord. No instruments used. | Both corneæ reported by accoucheur as "opaque" at birth. P.M. Slight evidence of inflammation of R. cornea. No stripes. | Great head moulding, and distortion of face. | Abrasion of skin over ramus of R. lower jaw, probably due to the promontory. | Stillborn. Sex? Weight? | Here we have an example of slight damage to the eye in an unassisted but complicated labor which ended fatally for the child. |

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| CASE H ..... Thomson, age? (Thomson and Buchanan, *Ophthalmoscope*, 1905) | Primipara. C. V. 3 inches. 1st, 2d, and 3d stages, 11 hrs. and 20 min. Vertex P. Forceps applied twice. Position of blades? | R., vertical stripe. P.M. showed extension tear of Descemet's membrane. L., general corneal haze. | L. eye proptosed at birth. | ..... | Stillborn. F. 9½ lbs. | Case reported to us by Dr. Jardine, who obtained one eye for examination. |
| CASE J ..... Moffat, Age? (Thomson and Buchanan, *Ophthalmoscope*, 1905) | Primipara. C. V. 2¾ inches. 1st and 2d stages, 23 hours. Vertex P. "Difficult delivery." Forceps at brim: (1) right frontal bone; (2) left frontal bone. | Opacity of R. cornea at birth; 2nd day, horizontal stripes noted in addition; 5th day, stripes marked by general opacity; 9th day, stripes reappeared, general opacity diminished. Appearance at 4 months as in drawing, Fig. 5. | Great head moulding. | ..... | Living. F. 5¼ lbs. *Child's head:* BT., 3 inches; BP., 3⅛; SOB., 3⅛; OF., 4. | One of the few cases in which the corneal stripes are not nearly vertical. 11 months after birth, the linear opacities, though narrow, were still distinct. |
| CASE K ..... Molloy, aged? (Thomson and Buchanan, *Ophthalmoscope*, 1905) | Primipara. Pelvis normal. 1st and 2d stages 36 hours. Vertex P. Forceps at brim: (1) left forehead extending down to eyebrow. | On 6th day, whole L. cornea slightly dull and presenting two narrow vertically placed curved stripes which enclosed the pupil between them; as in drawing, Fig. 6. | None noted. | Ecchymosis conjunctivæ. | Living. M. 9 lbs. | Pelvis said to be normal, but the size of the child determined a prolonged and difficult labor. |
| CASE L. ..... Mrs. X., age? (Thomson and Buchanan, *Ophthalmoscope*, 1905) | Primipara. Pelvis said to be normal. Occipito-posterior P. "Difficult delivery." Forceps at brim: (1) over the R. forehead; end of blade extended down to and abraded upper eyelid. | On 6th day, general opacity of R. cornea. By 23d day, vertical linear opacities were visible. | None noted. | Curved abrasion of upper eyelid corresponding to shape of end of forceps blade. | Living? Sex? Weight? | Another case of severe corneal lesion when the pelvis was not contracted. Case seen in private practice. |

TABULAR STATEMENT OF TWENTY-TWO CASES OF BIRTH INJURY OF THE EYE.—*Continued.*

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|---|---|---|---|---|---|---|
| Case M ..... Watson, aged about 25. (Thomson and Buchanan, *Ophthalmoscope*, 1905.) | Multipara. C. V. approx. 3¼. 2d stage, 2½ hours. Vertex P. "Very hard pull." Forceps; bitemporal at birth, but had been removed and reapplied. | At 3 weeks, L. cornea presented two incomplete linear opacities almost in same vertical line. | Fracture of the skull. | ? | Living. Sex? About 7 lb. | With exception of the corneal lesions, which we saw at 3 weeks, the particulars are from memory of obstetrician. |
| Case N ..... Mrs. A., aged 26. (Thomson and Buchanan, *Ophthalmoscope*, 1905) | Multipara. C. V. 3⅛ inch. 2d stage, 5 hours (induction of premature labor). Vertex P. Details regarding forceps wanting. | At birth, R., three vertically placed barrel-stave-like stripes; general opacity. L., one vertical stripe; general opacity. | Proptosis of L. | ? | Stillborn, premature. Sex? 6½ lbs. | Case related by Dr. Jardine and not seen by us. Pressure on L. side of head by promontory and on R. by forceps. |
| Case O ..... Mrs. McK ——, aged? (Thomson and Buchanan, *Ophthalmoscope*, 1905.) | Multipara. C. V. 4 inches. 1st and 2d stages, 18 hours. Vertex P. "Difficult delivery." Forceps at brim: (1) outer edge of R. orbit; (2) left temple. | At birth, general opacity of R. cornea and two close-set vertical stripes. General opacity increased, then diminished and left one vertical linear opacity. | None noted. | At birth, fluid blood in R. ant. chamber, some of which eventually adhered as a clot to the centre of the post. corneal rupture. | Living. M. 7 lbs. BP. diameter of head, 4⅛ inches. | A large head seems to have been the main determining cause of a difficult labor. Position of forceps suggests pressure on both orbits, but only one eye was injured. |
| Case P ..... Kelly, aged? (Thomson and Buchanan, *Ophthalmoscope*, 1905) | Primipara. Dwarf. C. V. 2¾ inches. Pelvis not much deformed. Vertex P. "Delivery not very difficult." Forceps at brim: (1) R. forehead; (2) L. mastoid. | At birth, L. cornea hazy. This general opacity increased and then cleared up. On 12th day, narrow obliquely placed linear opacity, up and out to down and in. | Proptosis of L. eye which disappeared about 8th day. | Wound of skin near R. outer canthus. | No particulars. | Note: There was no forceps blade near the injured left eye, and the corneal rupture is in a plane at right angles to that in which the head was compressed by the forceps. |

Fig. 1.

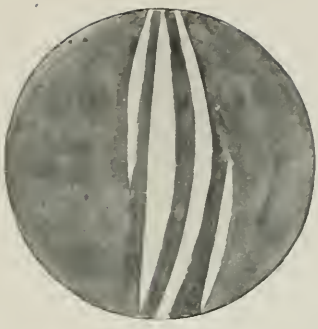

Diagram of the posterior surface of the cornea of Case A. The dark coloration represents blood on the posterior elastic lamina. The light bands show where the elastic lamina is ruptured.

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Fig. 2.

Meridional section of the cornea of Case A magnified 15 diameters, showing three of the ruptures. Two of them show involvement of corneal lamellæ, the third interruption of posterior elastic lamina only. The layer of blood is also visible. The floor of the concavity formed by retraction of ruptured corneal lamellæ is smooth. Repair has commenced and the ruptured fibres are sealed down by fibrin.

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| Case Q ..... Cammidge, aged 21. (Thomson and Buchanan, *Ophthalmoscope*, April, 1907.) | Primipara. C. V. 3⅞ inches. 1st and 2d stages, 22 hours. Vertex. P. "Difficult pull." Forceps at brim: (1) over left parietal, frontal and temporal bones, with tip of blade on the edge of the lid; (2) over R. mastoid. | At birth, two vertical parallel narrow stripes; general opacity quickly came on 2nd day, cornea seen to be oval horizontally; consid. general opacity; striping faint. 7th day, corneal ulcer opposite lid abrasion. | Proptosis of left eye. | L. upper lid abraded neat ciliary border by tip of forceps blade. Ecchymosis conj. L. facial paralysis, supposed by accoucheur to be due to pressure by the promontory. | Living. M. 6 lbs. *Head:* BF., 3 inches; BP., 3½; BT., 3½; SOB., 3½; OF., 4½. | Long labor. Distinct evidence of forceps pressure on orbit and on eye itself. Corneal ulcer took a long time to heal. |
| Case R ..... McHugh, age? (Thomson and Buchanan, *Ophthalmoscope*, 1907) | Multipara (8). C. V. 4 inches. All previous labors difficult and instrumental. Vertex P. "Labor very prolonged." Forceps at brim: ? bitemporal. | At birth, vertical stripe seen in R. by accoucheur. 6 hours later, cornea steamy no stripe (T. and B.). 10 hours later, opacity greater, no stripes. | ? Fracture of skull. | Ecchymosis conj. | Particulars wanting. Died in 24 hours. No. P.M. | Some points in obstetric history: one child stillborn, head crushed; one died in 24 hours; two had cuts on the temple; and the present case. |
| Case S ..... Gilmour, aged 30, (Thomson and Buchanan, *Ophthalmoscope*, 1907) | Multipara. C. V. 3¼ inches. 1st and 2d stages 13 hours. Presentation V. Forceps at brim: (1) over R. eyebrow encroaching on lid; (2) over L. mastoid. | R., faint corneal haze, which disappeared in a day or two. | None. | Thin layer of blood on surface of the R. iris. | Living. Sex? 7½ lbs. | A case of transitory corneal opacity, a condition probably often overlooked. |
| Case T ..... Kerr, aged? (Thomson and Buchanan, *Ophthalmoscope*, 1907) | Multipara (5). Cont. pelvis. Previous labors all instrumental; three out of four terminated fatally for child. 2d stage, 9 hours. Presentation transverse, with arm down. Arm replaced; forceps to head. "Great difficulty" in delivery. Forceps at brim: (1) over R. forehead, tip of blade at orbital margin; (2) behind L. ear, tip of blade on neck. | ..... | At birth, R. eye dislocated forward; was replaced by accoucheur. Seen by T. next day. Conjunctiva torn and stump of int. rectus presenting. Eye bloodless, cornea steamy; eye dislocated on separating lids, held apparently by optic nerve and external rectus. Excision. Orbit contained no quantity of blood; no bleeding on severing remaining connections. | ..... | Living. Sex? weight, average. | From the fact that there was no evidence of hæmorrhage into the orbit and that the optic nerve was intact, it is probable that in this case the eye was simply forced out by diminution in size of the orbit; and that the muscles and vessels were ruptured by extreme stretching so that bleeding did not occur. |

# EXTRACTION OF CATARACT IN THE CAPSULE

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The subject of Cataract-Extraction is, to judge by the frequency with which it is discussed in Ophthalmic Societies and Congresses, one of predominant interest to every ophthalmic surgeon, and one moreover in which the last word has not by any means been said.

In Asia and other tropical and sub-tropical parts, where cataract is immensely more frequent than in temperate climates, there is still considerable difference of opinion as to the best mode of treatment, and surgeons of almost equally great experience are to be found in both of the main camps; one of which stands for advocacy of extraction in the capsule entire, and the other for the capsule-laceration method by which the lens is first removed, and subsequently the cortex matter got rid of either by stroking the cornea directly or through the lower lid, or by the use of instruments such as forceps and irrigator within the eye.

Such an experienced operator as Major Herbert, of Bombay, is strongly convinced that to attempt the removal of the lens in the capsule entire is unjustifiable as a routine procedure, holding that, "the operation violates the essential conservatism of correct surgery in that it introduces unnecessarily a risk, *i.e.*, for the sake of advantages which can be obtained without risk."[1]

On the other hand the unique ophthalmic experience of Smith of Jullundur by whom the operation has been perfected and whose name it now generally bears, goes far to show that the risks in careful hands are not appreciably greater than in the capsule-laceration method of operating, while the immediate results are better, and the patients are much freer from the likelihood of the after-complications which beset the older operation, and which so often bring disappointment to both patient and surgeon.

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[1] *Indian Medical Gazette*, February, 1906, p. 51.

I think that most surgeons of more moderate experience will be disinclined also to regard the after-complications of the capsule-scratching operation with the equanimity which the above quoted statement expresses. We rather feel tempted to break the Tenth Commandment when we hear of a surgeon who has reached the position where iritis, irido-cyclitis, and after-cataract are regarded absolutely as "without risk."

I desire in this paper to describe, first of all, Smith's operation in some detail, because it varies distinctly from that performed by Pagenstecher, and is almost passed over in the majority of text-books, or at most has a few lines devoted to it. This seems a distinct omission when the operation is performed so frequently in the countries where the opportunities for experience in cataract work are extraordinarily large. The surgeon whose name it bears has performed it some *fifteen thousand times,* I understand, and there are a large number of other surgeons who employ the method in the majority of their cases.

In such a highly delicate operation it is the observance of small details which make or mar its success, and I am sure, judging from my own past experience, and from conversations with other surgeons, that what has been performed as Smith's operation, is very frequently not the operation which Smith himself describes.

In the second place I desire to discuss and contrast to a limited extent the two operations.

I would here mention that I have had the advantage of seeing Smith himself perform his operation nearly 200 times, and I quickly learned that what I had been accustomed to perform as his operation was different in several important particulars, and these particulars were exactly those things which, to a large extent, obviated the risks that are ordinarily regarded as the drawbacks to an otherwise brilliant operation.

A preliminary word must be said as to the patients on whom it is performed. They are, in the main, the usual class which constitute the out-patient clinic of a large Indian Hospital, and are gathered from villages all over and beyond the Panjáb. They are agriculturists, small shop-keepers, Government clerks, and the wives of such people. The majority are Muhammedans. The argument has been made that the operation is only possible where the

patients are exceptionally obedient and self-controlled, and therefore, reasoning backward, as it is performed more in the Panjáb than elsewhere, that the Panjábi must excel in these admirable qualities.

Having lived and worked in the Panjáb, as well as in two other Indian Provinces, and having seen the great daily clinic at Jullundur, I am persuaded such an argument is baseless. These people have neither more nor less of self-control than other Indian patients, *except in so far as the way they are dealt with conduces to the preservation of any little courage they may have.*

It is certainly astonishing as well as something of a shock to one's aseptic principles to see 50 or 60 Indian eye patients of the usual dirty type, sitting around in the room, where, with open doors, the operations are performed; and it is not less surprising to appreciate the quietness with which the whole operation proceeds without the patient being asked to aid in any way, either by looking up or down.

One becomes convinced that the performance of the operation within sight and hearing of their friends, goes very far with this class of people, toward giving confidence and calm to the person operated upon. The hurrying off of a nervous superstitious man into a room furnished with strange and awesome appliances, while the door is shut upon his friends and acquaintances, and he is left alone mainly with those who speak his language imperfectly, is certainly well calculated to disturb such a person's equanimity, frighten him, and unfit him for doing the various things which are peremptorily asked of him.

After the novelty of the sight has worn off, one sees that though it struck one as contrary to aseptic principles yet it works out successfully, because everything touching the eye itself is most rigidly sterilized, otherwise the success would not be so great as to draw nearly 3000 persons in one year to the hospital to have cataracts removed.

Furthermore the success is not to be found in the meteorological conditions, for the Panjáb rejoices in a climate where everything is covered with a fine dust for nearly eleven months of the year, and dust storms are extremely frequent and violent. It is therefore an exceedingly *bad* climate for performing *eye* operations.

### THE PREPARATION FOR OPERATION

The patients, who have often walked long distances to the hospital, are almost without exception operated on the morning they arrive. It would be better to keep them for preliminary treatment, but in most cases they would go away and never appear again if this were suggested. When put on the table, the outside of the eyelids, the brows, cheeks and nose are rubbed vigorously with swabs of 1 in 20 carbolic lotion and dried. Several drops of 4 per cent. cocaine solution are instilled, and in a minute or two the operation is begun.

The instruments are made ready by being soaked in 1 in 20 carbolic solution for an hour or two before the operation. They are usually removed and put in a mug of 1 in 40 carbolic when the operation is about to commence. The knives and some fine instruments are, however, taken from and returned to the tray of 1 in 20 carbolic. A vessel holding two or three gallons of 1-2000 corrosive sublimate solution is swung up to the ceiling, 7 to 8 feet above the level of the patient, and connected with a wide diameter ($\frac{5}{8}$ or $\frac{3}{4}$ inch) india rubber tubing with clamp.

*The operation,* is commenced by inserting the speculum (a spring one, without any cross-bar or fixation screw is usually employed by Smith), which is held up by an assistant while the fornices are vigorously douched with the 1-2000 lotion coming with considerable force from the container above. This is continued for about 15 seconds, but coming from such a "head" of water it seems effectually to sweep out all mucous from both lids even better than swabbing with pledgets of wool. The speculum is let down again upon the eye, and the conjunctiva is seized by fixation forceps close to the cornea at its lowest part, and the bit seized is twisted half round so as to steady the eye better and to prevent it from tearing away. One of Weiss' v. Graefe knives (which with care seem capable of making 70 to 100 incisions before needing to be set) is used to make the incision. The point is inserted on the temporal side 1 or 2 mm. above the horizontal meridian of the cornea, beginning at the junction of sclero-corneal tissue "just as deep as anatomy and experience teach us will avoid wounding

the vessels of the dangerous area." [2] Both eyes are incised with the knife in the right hand. For the left eye the surgeon stands beside the patient facing him and cuts away from himself.

The knife should be carried well through to the heel and swiftly across to avoid the iris falling in front. A cut is made in, then rapidly upwards dropping the handle towards the chin to avoid pricking the eyelid. If the counter-puncture seems likely to encroach too far upon the sclera, it can easily be brought out nearer the cornea by twisting the blade slightly on its back and dropping the handle a little before pushing it through. A corneal flap of almost half the diameter of the cornea is thus made which encroaches about $\frac{1}{2}$ mm. on the sclerotic at its commencement and ends in corneal tissue "about half way between a normal pupil and the sclero-corneal junction."[3] By a "normal pupil" is meant one mid-way between full contraction and full dilatation. In practice it comes to be about 1 mm. from the corneal-scleral junction. There is therefore no conjunctival flap. The making of a conjunctival flap is in Smith's opinion needless as the cornea heals rapidly.[4] It, of course, could be done if so desired without an interference to the operation except from the bleeding, which, however, could be almost obviated by using adrenalin with the cocaine drops as many of us do as a routine procedure.

An iridectomy is now made. Formerly this was dispensed with, and certainly the lens can easily be extracted without it. To do so is a somewhat slower process as pressure must be maintained until the iris muscle is tired out, and then the lens emerges easily.

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[2] *Indian Medical Gazette*, June, 1901, p. 222.

[3] *Indian Medical Gazette*, June, 1901, p. 222.

[4] As an instance of how readily corneal tissue adheres and heals, the following case occurred in my practice while writing this. A patient was operated on at 2.30 P.M. one day. The operation was hurriedly concluded owing to an assistant, new to the work, letting go the lids before being told. Vitreous appeared, but receded, and the lens slipped back out of sight. No more was done then. The next morning at 9 A.M. the lens was close behind the pupil having apparently floated up when the anterior chambered refilled. It was safely extracted and the patient did well. What impressed one was the very firm adhesion of the lips of the corneal wound. The knife had to be used almost precisely as if making the incision for the first time. Separation of the lips by a blunt spud, as is sometimes described, was quite impossible. A conjunctival flap could hardly have healed more quickly.

But prolapse of the iris occurs more often where an iridectomy is not done, and this in a hospital pressed for time and short of assistants, means more attention to the case, so as a matter of routine safety iridectomy is now adopted.

In almost every case this is accomplished without the entrance of an instrument into the eye. The iris forceps are taken and one limb is made to dimple in the cornea close to the free edge of the wound. This tips the corneal edge away from the iris which is revealed below it. Then the other limb, which is resting on the sclera above the wound, is approached while the limb on the cornea slides off the cornea on to the iris, is thus lightly caught in the grasp of the instrument and gently drawn out until the pupillary margin is outside, when the iris is snipped off. The manœuvre requires a little practice, but is worth while, as the risk of another instrument entering the eye is obviated. If unsuccessful, it can readily be done in the usual manner. Of course, care is taken in any case to avoid giving pain, by squeezing the iris and so causing spasm of the orbicularis muscle.

The speculum is now removed and taken away. The eye is closed and the finger is gently passed over the closed lids from nasal to temporal side thus sweeping out all fluids such as aqueous and blood, and leaving a clean field.

Now comes the most important duty of the assistant, which, until he is trained to do well, makes the operation difficult in its subsequent steps. He, standing by the side of the patient, facing him, holds the patient's head between his two hands so as effectually to prevent involuntary movement. In performing a cataract operation on the right eye, the assistant's left hand rests on the patient's face, and the thumb draws down the lower lid firmly. If the face is moist a piece of gauze between the thumb and face will make the hold better. The ulnar border of the right hand rests on the forehead in such a fashion as to push upwards the occipito frontalis and orbicularis muscles of brow, while the assistant's thumb and forefinger are employed in holding up the upper lid with a strong strabismus hook inserted underneath the upper lid on the temporal side. The upper part of the orbicularis is "unrolled," so to speak, and held well upwards so as to leave ample space for manipulation beneath the upper lid as described further on. The

assistant *must not relax in any way* his double hold until the operation is concluded, and he must use his hands so as to keep the patient's head firmly locked between them, while attending to the lids as described.

The operator, in doing a cataract operation on the right eye, standing at the end of the table above the patient's head, now places his left hand so that it rests near the root of the patient's nose and with that hand, holds up the nasal side of the upper lid by a cataract spoon or scoop, underneath the upper lid, which enlarges the field still more, and also keeps the instrument ready and near in case it is required. He does *not* use it, however, in any way for counter-pressure, and this absence of counter-pressure is another important feature of the operation for minimizing the likelihood of the escape of the vitreous.

With the strabismus hook in the right hand applied over the cornea at the junction of the lower with the middle third of the lens, the expression of the lens in capsule is commenced. Pressure is made by the convexity of the hook slightly toward the back of the eye until the lens begins to present in the wound. The pressure is maintained as before and is combined with slight pressure toward the lips of the wound, thus following up the lens very slowly. This is often combined with a slight rocking movement of the hook on its convexity, so as to free the periphery as well as the central portion of the encapsulated lens. If difficulty is experienced in getting the edges through the wound, the hook may be turned (maintaining pressure against the cornea while turning it, so that the dislocated body should not slip back again), and the blunt point is pressed on the cornea to free each side. The actual expression must be done without the least haste, and the pressure used must be slight but continuous until the end.

The operator is careful to keep the wound plugged, as it were, by the out-coming lens, and so guard against the vitreous escaping, for if this occurs before the lens is out it is a much more serious matter than the loss of a drop or two after the lens has been extracted. In very large cataracts, where difficulty would be experienced in delivery through the wound, an attempt may be made to tilt forward the upper edge of the capsulated lens, and make it turn on its horizontal axis, thus falling over on the front

Fig. 1

The man on left side of picture represents the surgeon, who, with his left hand, would hold up temporal side of lid with flat scoop or spoon. His right hand (not visible) would be free for applying pressure to cornea with strabismus hook. The assistant holds up nasal side of lid with strong strabismus hook, grasping patient's head firmly between his two hands, holding down lower lid with left thumb, while his right little finger "unrolls" and holds up arbicularis. (In illustration the assistant's thumb is too far from lower lid to control it properly).

of the cornea. This is done by stroking the convexity of the hook downwards, toward the lower lid, while at the same time light pressure is made back toward the retina. When the lens tilts forward it is followed up in the manner described. This manœuvre often succeeds in getting a large lens safely delivered without breaking the capsule.

*In any case the expression of the lens should be a much slower process than in the capsule tearing operation.*

During all these procedures the patient is not asked to look down, nor indeed is spoken to at all. As a rule, with such patients, it is excessively difficult to get them to do what you ask at the moment you want it, and the asking invariably makes them more nervous and less self-controlled.

The majority of eyes assume the position of greatest ease, and of least tension, that is, they look high upward into the superior fornix, as in sleep. This is a position of considerable difficulty for the surgeon, *but of greatest safety to the patient.* Indeed, I think that in every case where I have seen vitreous escape, it was in patients who insisted on, or were asked to, look downward. But with a thoroughly intelligent assistant holding the lids as mentioned, the surgeon assisting with his spoon, a clear field is obtained quite sufficient to do the extraction and one considerably larger and under better control than can be obtained by a Desmarres' retractor which would take up more room than the hook and spoon.

The lens having thus been safely expressed in its capsule, any tag of iris protruding is reposited with the blunt hook point and the eye is closed. Once again the finger is passed gently over the closed lids to sweep out any blood, etc. It is then opened for a second to see that all is well and finally closed. Atropine is not instilled as a rule, but only when there is some definite indication for it, which is rare. Iodoform and boracic powder are sprinkled over the closed lids of both eyes (even where only one cataract has been extracted), a piece of white gauze, soaked in 1-2000 mercury lotion, is laid across both eyes, the hollows are carefully padded with alembroth wool, and two turns of the bandage over both eyes completes the operation. The patient is invariably carried to bed.

In the majority of cases the operation has been done from first to last with the entrance of only one instrument into the eye and

that a knife, which is the least likely of all to carry infection from without. Traumatism to the iris by introduction of forceps or irrigator to extract the capsule or soft matter is avoided; and of course after-cataract, with the disappointment it causes to both patient and surgeon, as well as the risks, slight though they are in the majority of cases, which its treatment entails from the capsule left behind, is impossible.

As to the larger body bruising the iris in its progress outward, it is found in practice that iritis is rarer with this operation than with the older method. It may be presumed, therefore, that iritis is due rather to matter left behind to be absorbed and to the passage of instruments into the anterior chamber, than to the gradual passage of a smooth body over its anterior surface.

*Accidents.*—Accident number one is *escape of the vitreous,* and because of its frequency, the extraction of cataract in the capsule has been regarded as an unjustifiable risk, and has been abandoned by many surgeons. Even so skilled an operator as Major Smith cannot eliminate this accident altogether, but I believe that if his methods are closely followed, the percentage of cases will be very small. Smith is confident that by roughly choosing his cases he could bring the accident down to 2 per cent. In practice in India, however, it is higher than that, because wherever there is a chance of giving some sight to a man, who often otherwise would be helpless as a bread-winner for his family, Smith operates even though it be an unfavorable subject from other points of view. In his ordinary clinic, however, where the cases were not specially selected, I saw 71 consecutive extractions before an escape of vitreous occurred. In the majority of cases the vitreous appears as a mere bead just after the lens has escaped. It is cut off level with the eye-ball and seems to make not the slightest difference in the after-progress or visual acuity.

When, however, vitreous escapes before the lens is out, it is likely to be a serious matter, especially if the escape is in considerable quantity. Even when this occurs, presuming the lens is easily got out, it is surprising to find what a comparatively large amount of vitreous may be lost without materially affecting the patient's recovery. If, at the same time, the capsule bursts, the mixture of vitreous and soft matter is very prone to give rise to trouble.

Whenever the vitreous appears, no time should be lost in slipping the scoop or spoon, which is being used by the surgeon to hold up the upper lid, under the lens, pressing up toward the cornea to keep the lens from slipping away and gradually drawing it out with the lens upon it. This is really what Pagenstecher does intentionally after making his incision. If it comes out without the capsule rupturing and with little instrumentation the prognosis will be good. Any tag of iris which does not easily come away had better be left alone, for it can be dealt with later, and if much manipulation is attempted, this is certain to result in further escape of vitreous. For the same reason soft matter, in the case of the capsule breaking, had better be left unless it comes away quite easily. The assistant then lets down the upper lid first, very gently, and not until it is in place does he relax his hold of the lower one.

The second accident which may occur is *rupture of the capsule before the lens is delivered.*

This usually occurs just as the lens is extruded and is half-way or more through the wound. In such cases one is in a position which offers little more difficulty than the ordinary operation, excepting that the rupture may not be so favorably situated as would have been the case if the laceration had been made with the cystitome. It is important, however, when the accident happens, to keep up sufficient pressure with the strabismus hook to prevent the capsule, which is disclocated, from retracting with the soft matter.

Smith recommends an ordinary pair of dissecting forceps to get a good broad and gentle hold of the capsule which is protruding, and with a slight to-and-fro movement it can often be easily drawn out along with the contained lens matter. If that fails, the cortex must be removed by irrigator or forceps as personal experience favors.

For my own part, I think the irrigator nozzle, introduced gently within the lips of the wound, seems to do less damage with its stream of saline solution floating out the substance than "fishing" about with iris forceps in the interior of the eye.

Personally I have grave doubts as to the transparency or innocuousness of retained capsule. After careful floating out of many

capsules in water, I have been unable to find more than a very few whose capsule, either posteriorly or anteriorly, could be called transparent, and I am inclined to think that even these few are liable, in the majority of instances, to become opaque to some extent in a short time when retained in the eye, the patient then being in the position of having a ground glass screen before his eye, necessitating a second operation for tearing it across. It is often difficult to persuade a patient to have this operation done, after his disappointment in the first operation, and if it is not performed the lack of good sight is put to the surgeon's discredit.

Summarizing, the following conclusions seem justifiable:—

1.—The operation of extracting a cataract in its capsule, as compared with the capsule-scratching method is, even in skilled hands, slightly more liable to be accompanied by escape of the vitreous, which, if considerable, is a most formidable complication. In most cases with due care and close attention to details this loss is very trivial, and as far as can be ascertained at present, does no appreciable harm. "The loss of a small quantity of vitreous is not a serious accident."[5]

2.—The capsule may burst during expression of the lens. The operation will then be finished in exactly the same way as an ordinary capsule-scratching operation, except that it is usually easier to remove the capsule which is dislocated along with the soft matter.

3.—As nothing is left behind, there is no danger of after-cataract and therefore the resulting good sight is not afterwards impaired from this cause; a condition which demands a second operation.

4.—For a similar reason there is no call for the introduction of several instruments into the eye and therefore liability to iritis, irido-syclitis, and striped keratitis is much less likely to occur. (The percentage is generally only half as much or even less.)

5.—The slightly larger wound necessitated may conceivably result in greater curvature of the cornea in healing. This is not *proved,* and could only be demonstrated by following a large num-

[5] See also Diseases of Eye, Hansell & Sweet, 1903, p. 338; Ophthalmology, Fuchs, p. 967; Encyclop. Medica Article "Cataract," by G. A. Berry, Vol. 2, p. 176.

ber of cases for a considerable time after both operations and testing for astigmatism. As far as I am aware this has not yet been done. The fact that Indian jewelers doing the finest gold filigree work with the spherical lenses with which they left the hospital, and not returning with complaints of failing sight seems to go far to disprove it.

6. It is the ideal operation for immature cataracts which are almost without exception easily expressed in the capsule, thus avoiding the risks of artificial maturation.

7. It usually allows the patient to leave the hospital earlier, because free in large measure from the after-complications which attend the older operation. This to a poor man at the time of harvesting or sowing, when every hand is needed, means a good deal, because so long as he is in a hospital (in India) it means that one or more of his family must attend him and prepare his food.

8.—Extraction in the capsule is a more difficult operation. The skill of touch and delicacy required should be gained through the performance first of a fair number of capsule-tearing operations before essaying the intra-capsular extraction. Many operators now reduce the risks very much by setting out to do the intra-capsular extraction but prepared to change to the other if the lens seems impossible to dislocate without considerable more force than they feel justified in employing, and to use the cystitome and scratch the capsule if bursting of a very big cataract, with risk thereafter of vitreous escape, seems imminent. There is certainly much to recommend this course. After the pressure has been maintained some time, even if abandoned for the other operation, it is usually found much easier to extract the lens as soon as the capsule is torn.

In countries where the people are very prone to avoid a second operation, it seems justifiable to run some of the risks of the more brilliant operation, which, if successful, will avoid the necessity of further operative procedures, and which proves an immediate as well as lasting benefit.

# HOW TO TURN BACK THE UPPER EYELID

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There is a knack about turning back the upper eyelid that ought to be familiar to every physician,—not only to the eye-specialist but to the general practitioner, who never knows at what unexpected moment he may be called on to perform this little operation for the extraction of the foreign bodies that so frequently lodge under the lid and give rise to a degree of distress so strangely out of proportion to their size. It ought to be frequently put in practice by the general practitioner, and should be performed by the specialist systematically in every examination of the eyes. It should never be omitted when a foreign body is suspected or when the conjunctiva is diseased. An oculist does not need to be told to do this, but many general practitioners do; for by removing a tiny foreign body buried in the conjunctiva of the lid, they may prevent very serious complications of the cornea in their patient, particularly when the latter happens to be a workman who always defers leaving his work and going to see a specialist until the last possible moment.

The turning back of the upper lid ought to be done quite automatically. Nothing but long practice enables one to do this in an instant and almost without the patient's knowing what has been done. This degree of skill is acquired little by little in ophthalmological wards. There you see it constantly done; but try yourself; and it is only after many efforts that you succeed in accomplishing this little manœuvre with the requisite dexterity.

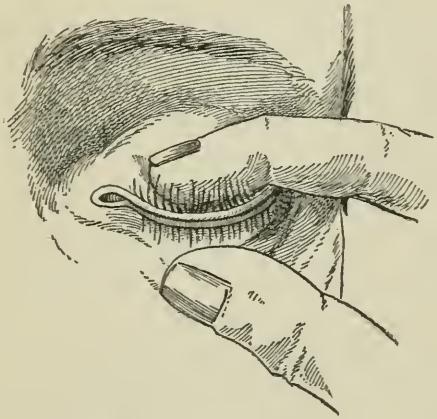
This rather tiresome period of apprenticeship might be much shortened if we were to pick the little operation apart into its component movements. The young practitioner would like to do it in a single movement, as he sees others do it; but the requisite skill is not to be acquired so quickly as that, and he makes his patients suffer, which is always undesirable. This separation of movements is more important still for the general practitioner

without experience in eye-practice; unless he proceeds in this way he will either not succeed in the manœuvre at all, or else he will put his patients to so much pain that they will not allow him to begin again.

The method of turning back the tarsus with a rod should be abandoned. We should always make use of the simplest, quickest and least painful processes in medicine. The fingers are the best instruments for the purpose, and two of them, thumb and forefinger, are all that are needed.

There are two ways of operating, according to whether the patient's eyelashes are abundant or scanty. In any event, if there is any acute disorder of the conjunctiva with blepharospasm, it is useful, and sometimes indispensable to drop two or three drops of a 2 per cent. solution of cocain between the lids.

FIG. 1.



I. *When the patient has abundant eyelashes.*—He should be seated face to face with the physician, who then asks him to look downward, and close the lids as though sleeping. This downward movement of the eye produces, by synergetic action, a lowering of the upper lid, which is absolutely indispensable though not altogether easy to obtain from the patient, who either does too much or becomes nervous and does too little. Some patients will thus look upwards, instead of downwards, carrying the lid upwards and rendering the operation very disagreeable if not impossible.

When this has been accomplished, what hand are we to use for turning the lid? The left for the right eye, and the right for the

left eye; always the hand contrary to the side of the eye, and one hand only,—two will simply be in your way.

Let us take the left eye, for instance:

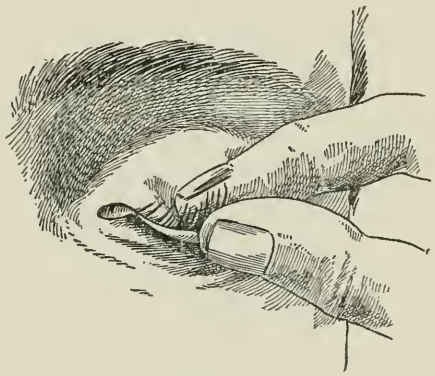
First.—Lay the ulnar edge of the right forefinger along the middle portion of the lid at equal distance between the inner and outer angles, just above the roots of the lashes.

Second.—Move this forefinger slightly upwards, still pressing on the lid.

This movement is destined by itself to produce a slight degree of ectropion of the edge of the lid (Fig. 1).

Third.—Apply the palmar aspect of the last phalanx of the thumb to the lower side of the lashes as close as possible to their base.

Fig. 2.



Fourth.—Seize the lashes between these two fingers, the index always remaining in close contact with the lid (Fig. 2).

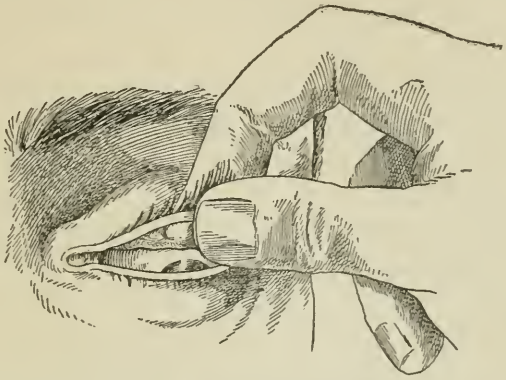
Fifth.—Draw the entire lid downward three or four millimeters.

Sixth.—Tilt the tarsal cartilage over backwards so as to hide its cutaneous face against the lid and bring its conjunctival face to the front.

*Method of performing sixth movement.*—When the lid has been drawn down, press with the ulnar side of the index finger, from in front backward and from above downward, against the upper edge of the tarsal cartilage, which can be distinctly felt. At the same time, and to help in the tilting movement, draw forward and upward the edge of the lid by means of traction on the lashes held

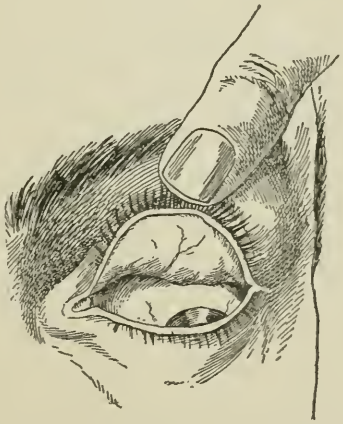
between the thumb and index finger. The two fingers execute a movement of rotation about a transverse axis passing through the point of implantation of the lashes (Fig. 3).

FIG. 3.



Seventh.—Hold fast the tarsal cartilage that has been tilted wrong face forward. To accomplish this the forefinger must be rapidly withdrawn, while, at the same moment, the thumb by a quick movement is carried backward and fastens the lashes against

FIG. 4.



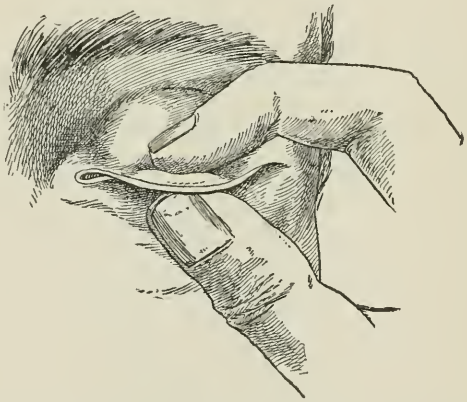
the skin of the upper portion of the lid beneath the upper edge of the orbit. The operation has then been effected and the inside of the lid can be examined with all the leisure desired (Fig. 4).

II.—*The patient either has scanty lashes or none at all.*—In this instance the increase in difficulty is not very great, if you know how to go about the manœuvre.

The patient must sit opposite you and look downward, as before. It is even more important than in the first case that there should be no tight shutting of the lids; that the movement of closing the lids should not be accompanied by any stiffness; that the articularis should be entirely relaxed, and that the lid should fall like an inert curtain.

Here again we only use the thumb and forefinger; but at this point the modus faciendi becomes different from what was used before. The turning out of the lid is a little more disagreeable for the patient, but this cannot be avoided, and he must necessarily put up with it. With persons whose sensitiveness is too great we can always fall back on a few drops of the cocain solution already referred to. Let us again consider the left eye.

Fig. 5.



First.—Apply the palmar aspect of the right thumb to the middle portion of the lower lid, push this lid backward and slightly upward as though trying to slide it behind the upper lid, between it and the ball of the eye.

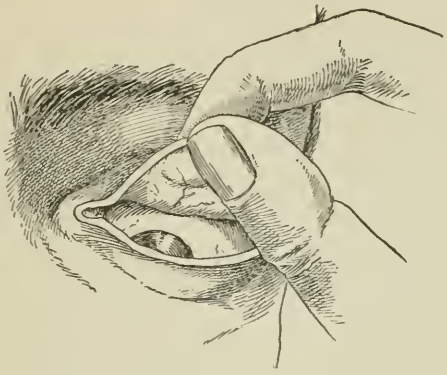
Second.—Apply the ulnar edge of the right index finger to the cutaneous surface of the upper lid midway between the two angles, three or four millimetres above the edge of the lid, and in the same vertical line as the thumb applied to the lower lid.

The index finger thus placed should press on the upper lid and bring it downward and slightly forward, in short, a movement exactly opposite to that used on the lower lid. When this has been done, the upper lid will have been brought down in front of

the lower lid, so that over an extent of two or three millimetres the conjunctival aspect of the upper lid will be in contact with the cutaneous aspect of the lower lid.

Third.—Move the thumb, which must remain in contact with

Fig. 6.



the lower lid, a little forward and upward so as to apply the ulnar edge of its palmar aspect to the upper lid over the portion of its conjunctival face that juts downward beyond the edge of the lower lid (Fig. 5).

Fig. 7.

When this has been done the upper lid is held by the thumb and index finger, and the thumb can consequently let go of the lower lid.

Fourth.—Tilt the tarsal cartilage upwards in practically the

same manner as in the former case, the only difference being that when there were eyelashes, we used them; now that there are none we use the conjunctival side of the lid's edge (Fig. 6).

Fifth.—Hold the tarsus in place when it has been turned over. Here again the movement is the same as that already described except that instead of having eyelashes with which to hold the lid in contact with the skin, we must press on the conjunctival face of the palpebral edge of the eyelid. (Fig. 7).

In a word, in either method we must: First, know how to get hold of the lid; second, prepare for the tilting movement of the cartilage; third, carry this movement out; fourth, keep the lid in place when it has been turned up.

If these separate movements are carefully rehearsed, and you take your time over the operation, especially at the beginning, you will soon perform it easily and without inconvenience to the patient.

Then little by little, with experience, the different movements gradually become but a single one, and, as I said at the beginning, you will turn a lid up automatically, and almost without the patient's knowing it.

# Neurology

## SOME CASES OF POLYNEURITIS (INCLUDING NEUROMYOSITIS) APPARENTLY NOT DUE TO ALCOHOL, ARSENIC OR ANY OF THE ORDINARILY RECOGNIZED CAUSES

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Even in regard to some such recognized causes of polyneuritis (multiple peripheral neuritis) as alcohol and arsenic the part they play in the production of the disease is by no means quite settled. It is notorious how few of those who indulge in alcoholic drinks develop polyneuritis, and in many cases it appears that the disease is provoked by two or more causes acting in combination. Thus, in the Manchester (1900) outbreak amongst beer-drinkers it appears to have been the combination of arsenic and alcohol in the beer which was mainly responsible for the symptoms; neither the alcohol consumed nor the amount of arsenic was usually sufficient, each acting by itself, to produce the neuritis[1] in ordinary individuals. Arsenic apart from alcohol, even when it produces very decided chronic arsenical symptoms, seldom gives rise to polyneuritis. This

[1] See the long discussion on Dr. E. S. Reynolds's "Account of the Epidemic Outbreak of Arsenical Poisoning," *Medico-Chirurgical Transactions*, London, 1901, Vol. 84, pp. 409-452. In a subsequent paper Dr. Reynolds (*British Medical Journal*, October 12, 1901, p. 1046) wrote: "I must confess that I cannot bring myself to believe that every case of alcoholic neuritis recorded has been really caused by arsenic, but I do believe that large numbers have been due to the combined action of alcohol and arsenic, and that arsenic in an alcoholic subject is much more virulent as a producer of neuritis than when taken alone. . . . . This combined action of drugs in producing neuritis was studied by Oppenheim in 1891, who pointed out the great susceptibility of metal workers to neuritis if they were also chronic alcoholics."

is especially noteworthy, as Sir W. R. Gowers and Dr. Thomas Buzzard have pointed out,[2] when arsenic is administered in combination with bromides for epilepsy.

Probably more attention should be directed to the fact that the cause of an attack of polyneuritis is often multiple, perhaps more often multiple than simple. Before pulmonary tuberculosis was recognized as an occasional (though rare) cause of polyneuritis it is almost certain that some cases were regarded as alcoholic peripheral neuritis which in reality were due to a combination of pulmonary tuberculosis, counterinfection with pyogenic microbes, and alcohol, the alcohol having been taken with the idea that it was "strengthening" and exercised an antagonistic action on the tuberculous process.

The relative frequency of the association of polyneuritis of the alcoholic type with pulmonary tuberculosis has been used as an argument to prove that alcoholism creates a predisposition to tuberculosis. There is indeed abundant evidence that alcohol often favors the development of phthisis, but it is now recognized that pulmonary tuberculosis is itself an occasional cause of polyneuritis of the alcoholic type, and therefore the occurrence of such polyneuritis in a consumptive patient is no absolute proof of alcoholism. In the same way now that it is recognized that tuberculosis may be an occasional cause of cirrhotic changes in the liver, the presence of hepatic cirrhosis in a consumptive patient can no longer be accepted as satisfactory evidence of the alcoholic origin of the patient's pulmonary tuberculosis.[3] I think that most cases of polyneuritis in patients with pulmonary tuberculosis are of the alcoholic type, and that the lower extremities are especially affected, but in a young man aged 27 years recently under my care for pleurisy, probably of tuberculous origin, weakness and wasting occurred in the muscles of the hands, apparently due to peripheral neuritis, though the lower extremities were only slightly affected.

It has, I believe, been suggested that the true and essential causes of polyneuritis of the alcoholic type in Europe are infectious, and that alcohol, etc., play merely a predisposing rôle in the ætiology.

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[2] *Medico-Chirurgical Transactions*, vol. 84, loc. cit.

[3] *Cf.* "Remarks on the Relation of Pulmonary Tuberculosis to Other Diseases," by F. Parkes Weber, *Lancet*, London, April 2, 1904.

Without going as far as this I would myself suggest that in many cases of apparently simple alcoholic polyneuritis there is an infective factor at the commencement. Thus recently in a patient with a somewhat bloated-looking face whose affection I was inclined to regard as ordinary alcoholic paralysis involving all four extremities,[4] I afterwards heard of the possible connection of the illness with a sore throat.

I will now proceed to certain cases in which the ætiology seems altogether obscure. The first of these cases I consider to be an example of multiple symmetrical neuromyositis rather than of ordinary multiple peripheral neuritis.

Case I.—This patient, with chronic œdema of both arms, I showed at the Medical Society of London on November 13, 1905. She was a married Jewess, aged 64 years, who began to suffer from swelling of the upper extremities about the middle of May, 1905. At the commencement of the illness there was apparently a period of some more general disturbance of the health, during the first day of which she suffered from pains in the legs. Otherwise the lower extremities seem not to have been involved. There was nothing specially noteworthy in the previous medical history. She had apparently enjoyed fairly good health, and had not indulged in excess of alcohol, neither could any evidence of arsenical or saturnine poisoning be obtained. The left arm began to swell about two weeks before the right arm. The swelling in both arms gradually increased and involved the hands (especially the backs of the hands, which became very œdematous), the forearms and the neighborhood of the elbows. The swelling was at first associated with much pain. For eleven weeks the pains were such that she could hardly sleep at nights. Then the pains became less troublesome, improvement commenced and the œdema gradually diminished. In November, 1905, there was little swelling remaining, but the shriveled and wrinkled appearance of the skin on the backs of hands still bore witness to a considerable amount of recent œdema. During the illness the movements in the joints of the upper extremities (hands, elbows and shoulders) had all become

[4] See F. P. Weber, "Acute Dilatation of the Stomach and Intestines in a Case of Multiple Peripheral Neuritis," *Edinburgh Medical Journal*, April, 1907, p. 315.

more or less limited, evidently from the formation of peri-articular adhesions. In some of the muscles the response to electrical stimulation was very deficient, and recently no contraction had been obtained in the muscles of the left thenar eminence, and the muscles of the front of the right forearm, even when galvanic stimulation sufficient to cause pain was employed. There was some muscular wasting in both forearms. There was no anæsthesia. The patient had not suffered from œdema of any other parts of the body. There was no evidence of disease of the thoracic or abdominal viscera. The knee-jerks were present, as were likewise the elbow-jerks and wrist-jerks on both sides. The pupils reacted to light.

In the discussion on the case at the Medical Society Dr. Risien Russell said he had seen a patient in whom peripheral neuritis was accompanied by similar œdema in all four extremities and in whom the œdema disappeared without any special treatment which could be regarded as the cause. In that case after the subsidence of the œdema there remained peri-articular thickening, adhesions and limitation of movements of the joints; and the electrical reactions revealed definite degenerative change, proving the presence of peripheral neuritis. In my patient, though no actual microscopic examination was made, I have little doubt that the muscles were affected as well as the nerves, in fact, that the case was one of "poly-neuro-myositis" rather than simply polyneuritis. In fact, the question arises whether most cases of polyneuritis when there is muscular pain and tenderness with œdema of considerable duration, are not examples of a certain amount of polymyositis combined with polyneuritis. The patient in question was subsequently lost sight of.

Case II.—Mrs. G. S., aged 30 years, a rather delicate-looking Jewess from Russia, was admitted under my care at the German Hospital on May 28, 1906, suffering from paralysis of both lower extremities with muscular wasting and typical foot-drop. Reaction of degeneration was present in the extensor muscles, and sensation was defective in both legs. There was no evidence of any disease in the heart or lungs, or in other parts of the body, and the urine was free from albumen and sugar. Two months before admission she had left Russia, and on the voyage to England the present illness had commenced with pains in the legs and "fever." She seemed

to be of a bright, cheerful disposition and had apparently enjoyed good health before the present illness; there was nothing pointing to alcoholism.

In the hospital she was treated by rest and good food, with massage and Faradism. She soon began to improve and was encouraged to make attempts to walk with the help of a "go-cart." Occasionally, even when she was improving, there were exacerbations of pain, during which periods she remained in bed. The temperature after admission only once reached 100°F, namely on the evening of her first day in the hospital. When she left the hospital, at the end of July, 1906, she could walk about fairly well with the help of two walking sticks, and there was less wasting of the muscles of the legs. The knee-jerks had of course not yet returned.

Case III.—The patient, a baker, aged 46 years, was admitted under my care at the German Hospital on January 1, 1903, for loss of power in all four extremities. The weakness in his hands and feet attracted his attention a month before admission, but otherwise he had not felt ill. He had been in the habit of taking beer and whisky, but did not at all give me the impression of an alcoholic. There was no loss of memory. *On admission* there was loss of power in the feet with defective sensation. He could walk, but owing to weakness of the extensors he had something of a "high-stepping" gait. The knee-jerks were absent. He could not stand with his feet together and his eyes closed. In the upper extremities there was some loss of power, but sensation was natural. The sphincters were unaffected. The pupils reacted well, and by ophthalmoscopic examination nothing abnormal was found in the eyes. There was no evidence of disease in the thoracic and abdominal viscera and the urine was free from sugar and albumen.

In the hospital at first the patient's condition gradually became worse. The sensation in the fingers became impaired as well as in the feet, and he could no longer walk at all. In the early part of February there was hardly any sensation in the right foot for touch, pain or temperature, and in the left foot also sensation was greatly diminished; the feet became œdematous. In March the patient began gradually, though slowly, to regain power in the upper extremities, but the œdema in the lower extremities was troublesome and the evening temperature was often about 100° F.

On March 30th, I noted that there was considerable œdema of both lower extremities and the soft parts of these limbs were decidedly tender to pressure. By about the middle of April the patient had so far recovered the use of his hands that he could use them for taking his meals. In May the power in the legs was slowly returning and the amount of œdema was less, but the latter varied considerably from time to time. After May 5th the temperature remained below 100° F. On May 25th in testing the electrical reactions it was found that there was typical reaction of degeneration to galvanic stimulation in the thenar and hypothenar muscles of both hands and in the muscles of both legs.

The treatment had been by electricity and massage, and for a considerable time Easton's syrup and small doses of potassium iodide had been used internally. After May 25th the progress was fairly steady, though occasionally there was œdema and tenderness in the lower extremities. He was soon able to get about with the help of sticks and with simple apparatus to correct the foot-drop. On July 30th there was still more or less anæsthesia on the plantar surfaces of the toes of both feet; in some parts of the legs there seemed to be hyperæsthesia. The patient was, however, at that time apparently subject to spontaneous feelings of burning or "pins and needles" in the feet, which somewhat complicated the testing of sensation. On September 21st the patient's gait was not yet quite normal, doubtless partly owing to weakness in the anterior tibial muscles in which ACC was still greater than KCC. He left the hospital about that time and I lost sight of him.

This case was partly described by my friend Dr. Leonard Williams (then my colleague at the German Hospital), who added that its interest and importance resided "in the possibility, which so seldom presents itself, of positively excluding not only both alcohol and arsenic, but every other factor to which the disease is usually attributed." [5]

Case IV.—Mrs. E. L., a married woman, aged 29 years, was admitted to the German Hospital under my care with more or less paralysis of all four limbs.[6] The history was that five weeks before

[5] *Practitioner*, London, August, 1903, p. 245.

[6] I have already described this case in *St. Bartholomew's Hospital Reports*, Vol. 34, p. 306.

admission she had a fright, and two weeks later she aborted. Since then she had not been able to get about. She suffered with pains and weakness in the limbs. *On admission* there was paralysis in both legs with "foot-drop," and there was likewise "wrist-drop" in both upper extremities. The sphincters were not affected. The paralysis resembled that of typical "alcoholic" polyneuritis, but the mental condition was normal, there was no loss of memory, and there was no history of the abuse of alcohol. The thoracic and abdominal viscera were apparently normal and there was no albuminuria. Under treatment by rest in bed, with galvanism and massage to the affected limbs, and small doses of strychnine, improvement was soon noted. At first the patient could not feed herself, but she soon recovered the use of her upper limbs sufficiently for this purpose. The lower limbs, which from the commencement were more affected than the upper ones, were slower in their progress towards recovery. After some time she was able to walk easily with crutches, provided that the feet were kept from dropping by replacing the natural action of the damaged muscles of the front of the legs by plaster-of-Paris bandages or special elastic supports. When she left the hospital, between three and four months after admission, she could walk to some extent without support of any kind and without any kind of apparatus.

This case is an example of polyneuritis connected with pregnancy, but apparently without any distinct septic infection. I include it here because of its obscure pathogeny, although the existence of puerperal polyneuritis without septic trouble is well recognized.[7] My friend Dr. M. H. Spencer has kindly told me of a case occurring in a woman about 30 years of age, in which there was likewise no suspicion of alcohol as a cause. In regard to less severe forms of puerperal polyneuritis Münchmeyer[8] recorded the case of a young woman in whom the symptoms of neuritis in both legs set in on the seventh day after childbirth, the pregnancy and labor both having been normal. There was loss of

[7] Of course one must bear in mind the possible occurrence of lead palsy after abortion in which diachylon has been used as an abortifacient. See Dr. W. B. Ransome's paper in the *British Medical Journal*, 1900, June 30, 1590, and later communications on the subject in the same Journal.

[8] *Centralblatt für Gynäkologie*, 1900, No. 49.

sensation in the legs with loss of knee-jerks, and there was likewise disordered sensation in the region of both ulnars. The symptoms in that case subsided in a few days without special treatment. E. Hauch (of Copenhagen)[9] describes cases of acute puerperal neuritis, shown by tenderness, pains, paresis, etc., in which the symptoms disappear in the course of a few days. R. von Hösslin [10] distinguishes several classes of puerperal neuritis and under the heading "puerperal toxic polyneuritis" includes some cases in which the symptoms arise before childbirth and in which, if the mother's life were threatened or if a rapidly progressing optic atrophy were recognized, the pregnancy might have to be artificially terminated.

Although, therefore, my case, No. 4, may be obscure in its ætiology, it at all events belongs to one of a series of clinical groups, but for my other cases even such clinical grouping is impossible, and it is worth noting that a writer in Russia (whence one of my patients had just come) has fallen back on so common a condition as chronic constipation in his search for possible ætiological factors in peripheral neuritis.[11]

In all cases of polyneuritis, even in those, as already mentioned, apparently due to alcohol, we have in the first place to consider the possibility of some infection (sore throat, etc.) which may have been overlooked. Thus Dr. F. W. Price[12] has recently recorded an example of very severe polyneuritis in a girl, 11 years of age, which followed on such a mild attack of scarlet fever that the latter might easily have been neglected in considering the history and ætiology of the case.

In the second place, however, the question arises whether some of the cases of polyneuritis in England, arising, like those I have described, in the absence of any of the recognized causes, may not be due, in great part at least, to a dietetic factor. Beri-beri,

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[9] *Zeitschrift für Geburtshilfe und Gynäkologie*, 1906, Band 57, Heft, 2.

[10] "Ueber periphere Schwangerschaftslähmungen," "*Münchener Med. Wochenschrift*, 1905, April 4, No. 14.

[11] A. Berstein, *Wratsch*, 1898, No. 29. Cf. L. Williams, *loc. cit.*, in regard to the obscure ætiology of some cases of polyneuritis.

[12] "A Case of Widespread Motor Paralysis Due to Multiple Symmetrical Peripheral Neuritis," *British Medical Journal*, 1906, 21st April, 914.

whether it is an infectious disease or not, is largely dependent on diet. This is well shown by its great diminution in the Japanese Navy brought about by the alterations in rations introduced by Baron Takaki.[13] The œdema and other symptoms in my case, No. 3, were remarkably like those of beri-beri, and œdema (though in the upper, not the lower, extremities) was perhaps the most striking symptom in my case, No. 1.

Eijkmann (of Utrecht), G. Maurer, and A. Treutlein have produced polyneuritis in fowls by feeding them on rice (rice without the husk), and probably there are other kinds of diatetic polyneuritis in fowls.[14] Whether such dietetic polyneuritis in fowls be really due to deficiency of lime salts[15] or, as Maurer and Treutlein think, to oxalic acid,[16] its occurrence is of great interest in regard to the ætiology in the human subject, not only of beri-beri but also of sporadic cases of polyneuritis of obscure origin.

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[13] See "Three Lectures on the Preservation of Health Amongst the Personnel of the Japanese Navy and Army," by Baron Takaki, *Lancet*, London, 1906, 19th May, etc.

[14] I suppose that a similar polyneuritis was the cause of the paralysis produced in fowls in Dr. D. Chalmers Watson's experiments by a raw meat diet. See his interesting paper on "The Effects of a Proteid Dietary (Raw Meat)," *Medico-Chirurgical Transactions*, London, 1904, lxxxvii, 531.

[15] Cf. remarks by Dr. E. I. Spriggs in the discussion on Dr. C. Chalmers Watson's paper on the "Effects of a Meat Diet on Animals," read before the Pathological Society of London, 18th December, 1906 (*Lancet*, 1906, 29th December, p. 1779).

[16] Cf. Dr. G. Maurer, "Polyneuritis der Hühner und Beri-Beri, eine chronische Oxalsäurevergiftung?" *Muenchener Medizinische Wochenschrift*, 1907, No. 15, 731.

# Dermatology

## PRESENT TREATMENT OF HYPERTRICHOSIS

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The discovery of the X-rays and their curious property of causing the hair to fall out, gave me hopes, as it did the majority of those interested in such subjects, that an easy and radical treatment of hypertrichosis had at last been found. This view is expressed rather emphatically in my last paper on the destruction of hair by electrolysis, published in October, 1897, in the *Annales de Dermatologie.*

I said at that time: "It is not yet too late to speak of the destruction of hair by electrolysis, although this process may quite well be, before long, one that has become superannuated. The latest experiments made with the X-rays have aroused the attention of every woman afflicted with hypertrichosis; I have already been applied to by several, who came to ask whether they could not try this form of treatment to get rid of the hair that annoyed them so greatly. But I did not feel authorized to advise them to do so. The method seems to me to be still enveloped in too many unknown quantities for any one, worried by the presence of hair on the face, to be told to expose that region to the action of an agent whose effect on the skin is in some cases terrifying; furthermore, we do not yet know whether the fall of hair produced by the X-rays is final and lasting, or whether, on the other hand, as everything seems to indicate, it is not merely transitory, and, in the latter case, what is the average duration of the period of re-growth. Still, it is true that the use of X-rays against hypertrichosis may perhaps have a great future before it, and, so soon as the method shall have been definitely regulated, may, with certain patients, replace with advantage the use of the various

destructive preparations on the market, and even lessen the indication for, or suppress altogether, the process of destroying hair by electrolysis."

This quotation shows that even so long ago as 1897 I thought, in view of the gravity of the accidents that strong applications of X-rays may produce on the skin, that we ought not to endeavor to obtain definite atrophy of the hair, but only a temporary depilation of considerable duration. But since that time science has progressed; means have been found of approximately measuring the amount of X-rays absorbed in a given time with a bulb of a given strength, and endeavors have been made to obtain, by means of the X-rays thus estimated in strength, total and definite alopecia without consecutive cutaneous alterations. It is certain that if this purpose can be carried out, the final treatment of hypertrichosis has been found; the only point is,—can it really be carried out.

Not to be accused of partiality I take the reply to this question from the treatise of Radiotherapeutics of Dr. Belot, (2d Edition, 1905). This author cannot, I think, be taxed with an attempt to restrict in an unwarranted manner the indications for X-rays. He says:

"The treatment of hypertrichosis by radiotherapy can only be effective if it fills two conditions: to produce final alopecia, and not to give rise to cutaneous modifications. The depilatory effect of the X-rays is too well known to necessitate further reference to it; but what ought to be known is that the hair grows again usually in from seven to ten weeks after depilation. This being true, the method is of less value than electrolysis, and if it is to be of any use at all, means must be found to prevent this re-growth.

"Nowadays we know how to remove the hair from a given surface, but we are never sure of producing permanent alopecia and at the same time preserving the integrity of the skin.

"The latter point is the key to the whole situation. Hypertrichosis is not a disorder, but merely a matter of personal appearance; our purpose is to restore the appearance of the face by removing the hair, but were this result to be followed by cicatrices, excess of pigment or dilated vessels, the patient's appearance not only would not be improved but would often be rendered more unsightly than before treatment. The problem can be stated as

follows, according to Freund: The ideal result will be produced when, during the entire treatment, the intensity shall have been regulated in such a manner that there shall never be any apparent change in the skin. Is it possible to obtain such a result?

"It is certain that in order to produce permanent alopecia the papilla must undergo atrophy or destruction. This can be done rapidly, giving rise to violent dermatitis; but such a result would be deplorable from an æsthetic point of view on account of the cicatrices, pigmentations and changes of color that would be left on a surface so treated.

"We are therefore obliged to make mild applications, which irritate or stun the papilla,—to employ Sabouraud's expression; and in this way to cause the hair to fall. Then, so soon as the hairs begin to appear once more, new applications must be made, of short duration, at more or less infrequent intervals, according to the extent and rapidity of the new-growth and the sensitiveness of the skin. In this fashion the papilla will be irritated, and little by little can be rendered incapable of producing fresh hair. This is the method recommended by Schiff and Freund.

"But can we be sure, even supposing ourselves able to estimate accurately the necessary quantity, of producing atrophy of the papilla, without the accompaniment of a little cutaneous atrophy? We are well aware that the hair-follicle is more sensitive to the X-ray than the skin itself; but is this difference sufficient to allow of the proper amount of strengths modifying the papilla without damaging the skin at the same time? This question is not an easy one to solve.

"In the opinion of Schiff and Freund, permanent results without scars can be obtained; but the treatment demands years. My experience, as well as that of many others, is far from being so encouraging. We can succeed in getting hair to fall from the face with the production of only slight erythema, but fresh growth is rapid. Treatment is then repeated, but after a certain time the hair reappears, and we must consider ourselves fortunate if, during these manœuvres, no modification occurs in the color or texture of the skin.

"For these reasons I believe that in this condition radiotherapy has not fulfilled the hopes to which it had given rise. In the present

state of our technical knowledge, we cannot be certain of obtaining permanent alopecia, and we must apprehend, in cases with specially sensitive skin, the production of lasting cutaneous lesions, frequently more unsightly than the hypertrichosis itself.

"Besides, with the exception of Schiff and Freund, the majority of practitioners, Béclére, Ehrmann, Kienboeck, among others, are not great advocates of the method, and radiotherapy has by no means replaced electrolysis in the treatment of hypertrichosis.

"For these reasons I feel that this method should only be used in serious cases. If a woman's face is covered with a thick, long and unsightly beard, a slight degree of cutaneous atrophy for such a patient will be less disagreeable than the original disfigurement. This method of treatment may also be resorted to when hypertrichosis takes the form of a dark and thick down."

This is what Dr. Belot has to say on the subject, and in my practice I, too, have observed the drawbacks to which he refers. I have seen patients who had undergone the X-ray treatment and who finally came and asked to have large hairs that continued to reappear in spite of frequent applications of radiotherapy removed by electrolysis. I have seen women for the time being disfigured by a vigorous application of the X-ray to the face for the purpose of removing the hair rapidly. And lastly, I have seen unfortunate women showing on different parts of the face, but particularly on the cheeks, permanent lesions of the skin, atrophy with vessel-dilatation, that had manifested themselves slowly and progressively after repeated applications of X-rays.

These facts have disturbed my mind to such a point that after having recommended radiotherapy to patients with extensive hypertrichosis from 1901 to 1902, I no longer feel warranted in giving such advice with confidence. I prefer to lay the whole question before them in detail, and to leave the choice of method to them after supplying them with full and minute particulars.

It is intentionally that I say "after giving them long and minute explanations," and I repeat it. Before deciding on a given line of treatment a patient must be told with precision what she may hope for, and what the drawbacks are that she risks. Such conduct on the part of the physician is only right, to begin with; but it is prudent as well,—for him.

Let us now take a brief glance at the various treatments in use for hypertrichosis, in addition to radiotherapy.

*Simple Eradication of Hair.*—Some patients, who have only a few hairs, and with whom the tendency of the down to develop into adult hair is not very marked, can secure the final disappearance of these hairs by pulling them out. There can be no doubt about the accuracy of this assertion, although such cases are very rare; but it is not safe to count on the success of this treatment when such advice is given to a patient with hypertrichosis however slight. To pull out a hair in the great majority of cases, is to give rise to a fresh one with a deeper and larger root. I have seen young women, who had had recourse to this method for a long time, finally reach a stage in which these hairs were enormous, their roots being buried in the hypodermis at a depth of four, six and even seven millimeters.

*Shaving.*—This is possibly even a worse method than pulling the hair out, as it acts both on the large hairs, whose vitality it increases, and on the down which it gradually brings to an adult stage. And yet it is really the only practical method for the unfortunate women with marked beards who cannot be treated by electrolysis or by radiotherapy. Some such patients shave twice a day.

*"Pilivorous" and Depilatory Preparations.*—In a general way I prefer shaving to the use of these remedies, which in many instances end by irritating the skin. True depilatory substances are sticks of agglutinating matter, which are applied to the skin and then suddenly ripped off in such a way as to tear out the hair and down that adhere to the preparation; their use is very painful, and they are much more pernicious than the elective removal of single large hairs with a pair of tweezers, since they tear out down and adult hairs without distinction and thus favor the transformation of this down into voluminous hair.

*Pilivorous* preparations are composed of elective pastes, of which the active principle is almost always sulphur, arsenic or lime, which are applied to the hairy surfaces for a length of time that varies according to the composition of the preparation, and that are washed off as soon as they have destroyed the hair to its point of issue from the skin. Here again the results of the method

are indiscriminate; it affects the down as well as the adult hairs, and the result of such application is almost infallibly a rapid and exuberant growth of the hair over the surface treated.

It is the use of these *pilivorous* preparations that is in the majority of instances the secondary cause of the serious cases of hypertrichosis of the face in young women. Annoyed at seeing down on their lip, chin or cheeks they apply *pilivorous* preparations, and little by little a full beard develops which has to be destroyed by electrolysis or radiotherapy. It is therefore advisable, when consulted by a young woman who has as yet nothing but down on her face, to caution her particularly against the use of these preparations.

*Peroxide of Hydrogen.*—For many years I have been using peroxide in light cases of hypertrichosis. Its advantage is, that it lightens the color of dark brown, renders it less visible, and, as it seems, dries it up, makes it friable, and checks its growth to a certain degree. For a long time, therefore, I have recommended it to young brunettes who are beginning to have an unpleasant amount of down on the face and arms. I usually combine it with frictions made with siccative powder, talcum, starch, carbonate of magnesia, etc., pure or associated with a little salicylic acid or sodium borate. When the hairs are coarse and very dark in color the peroxide is much less efficacious. In a word, it is only a palliative of no very real value, and I was astonished to see it recommended recently as having actual efficacy in removing hair. For my part I have never seen it remove down, and still less large hairs, in any one of my patients, although some of them have had recourse to it for many years.

There therefore remains electrolysis and radiotherapy as really efficacious methods of treating hypertrichosis. We have already mentioned the prevalent views as regards the value of radiotherapy at the present moment; but perhaps I may be of service to practitioners in giving them some advice about electrolysis.

*Destruction of Hair by Electrolysis.*—It is not my purpose to go into the technical details of this subject, for they can be found at the fullest length in my various publications. But I should like to put physicians on their guard against a mistake that, to the patient's detriment, is made daily.

My advice is often asked by women who come in great distress to show me white, punctiform scars on their faces between which a number of large hairs are scattered. They say that they do not desire any more electrolysis, because, after a certain number of painful séances, their hair continues to grow. "I had been told that the hair would be rapidly and finally destroyed; see for yourself what *your method* has done in my case," said one lady to me in despair.

The real culprits in these rather unpleasant cases are physicians who performed the operation and who committed two serious errors: First, they did not tell the patients what it was their duty to tell them before treating them; second, they operated too clumsily.

First.—Before beginning in a given case to destroy hair by electrolysis it is necessary, and this should in no instance be omitted, to tell the patient exactly what will take place. She must know that certain skins are of very fine texture, and that with them, no matter how well the operation is done, electrolysis may leave very small, punctiform, white spots. And it is particularly necessary that she should be told the mechanism whereby it will be possible to free her completely and finally from her deformity.

If, for instance, the case is one of marked hypertrichosis of the chin, when all the big hairs visible at the time of the operation shall have been destroyed the case is still far from being cured. Let us suppose, in order to take a concrete example, that at the beginning there are two thousand large hairs to remove. If the operation is well-done, that is, if the point of the needle is brought into exact contact with the root of the hair, and if neither too little nor too much current is allowed to pass, there will be about one or two out of ten hairs treated that will grow again, and eight or nine in ten will be permanently destroyed. It is then to be expected that from two to four hundred, out of the original two thousand, will grow a second time, and will have to be treated a second time; this is a first drawback to the operation of which the patient must be forewarned, and unfortunately it is not the only one. These two thousand large hairs, visible at the beginning of the treatment, form what I call the first crop. But Nature, extremely provident, has supplied the tissue of the chin with a remarkable power of producing adult hair. A month and a half or two

months after the destruction of the first crop of hair, new hairs, differing from the first, are seen to develop, with large fleshy roots, almost always very dark, and with slender free ends. The hair that grows afresh after having been already treated has its free end irregular or rounded. The new hairs emerge distinctly between the little punctiform white scars left by the destruction of the first crop. If the number of hairs of the first crop amounted to two thousand, those of the second will vary from eight to twelve hundred. And when the second crop has been treated, there will again be from one or two hundred that will reappear and that will also have to be retreated. Furthermore, one or two months after the disappearance of this second crop, there will appear still a third one, of three or four hundred hairs only, this time; and in many cases there is a fourth and even a fifth, each one less abundant than the one that preceded it. In order to obtain a satisfactory result all of these successive crops have to be exhausted with indefatigable patience, and when, at last, they have all been destroyed, at the end of a period which in the case of a well-defined hypertrichosis of the chin varies between one and two years, down will still be visible on the region treated. But all that is necessary at the time, taking even the most unfavorable hypothesis, will be to use electrolysis every four or six months on the hairs that seem more prominent than the rest, and recovery will at last be obtained.

What is true of the chin is, in a lesser degree, true of the upper lip, and of the edge of the cheeks, where three or four crops of hairs must be counted on. The neck, nipples and forearms give much more satisfactory results; in some cases a final result is obtained after the first treatment, but in any event it is rare to see more than two crops of hair.

If, now, in spite of the dryness of the technical details, you have taken the pains to read them, you will understand the despair and anger shown by women who, after they have undergone one series of painful and expensive operations, see "all their hair reappear," and you will also understand, the astonishment of the physician who, unaware of these details, immediately condemns the method as useless.

Let me emphasize again that it is indispensable, before beginning the treatment of a patient, to lay before her the various phases

through which she will have to pass, and to persuade her of the necessity of continuing the treatment to the end if she once begins, unless she wishes to run the risk of losing all benefit from what she has already endured. If, for instance, having six thousand hairs to be destroyed, she stops after five thousand have been destroyed, the remaining thousand will give the illusion of a beard that has not been treated, except for the scars that have been left if the treatment is not well done or when the skin is very delicate.

There is a remark that I am in the habit of making to those who ask me whether they can destroy hair by means of electrolysis: "This operation is a very easy one; any person, whether physician or not, can do it after a single lesson; but it is very difficult to do well."

The method consists, in a general way, in the following modus faciendi: A needle made of iridized platinum is inserted into the sheath of the hair until its point comes into contact with the root; the current should then be made to pass through the needle, which forms the negative pole; and the current must be interrupted as soon as the root is destroyed. That is all. But who is there who does not see at once how difficult it is to carry out this programme with absolute precision?

To begin with, the point of the needle must be exactly placed; for if it is not in direct contact with the root of the hair, too much of the surrounding tissue will have to be destroyed before the root is carbonized, and that will leave an unsightly scar; or else the root will escape altogether, and the operation will have been of no use.

Furthermore, the current must be turned on neither too long nor too short a time; if allowed to act too long, too much tissue is destroyed and a scar is the result; if not left on long enough, the root is not destroyed. Now, all these factors which play such an important part in the success of the operation, vary with the size of the hair to be destroyed, with the depth of the root, and with the degree of resistance of the skin, which, as we have seen, varies from patient to patient.

If in addition we consider that never in one sitting should two hairs be treated close enough to each other for the circles of destruction of the surrounding tissues to become tangent, under penalty of creating visible scars which may retract or form cheloids when

the number of hairs thus destroyed is large enough, it becomes easy to see that patients can be disfigured when electrolysis is badly applied.

Much the most delicate region to treat is the upper lip; the slightest technical fault here is at once followed by a very unsightly white cicatricial depression. But, once again, these faulty results are to be imputed to the operator and not to the process itself, and it is for this reason that, in my various publications on the subject, I have spared no pains to give full particulars and technical minutiæ; for this reason also, after much experience and many experiments, I advise that in all cases no more than the amount of electricity strictly required to destroy the root should be allowed to pass, for in the case of a woman, young and coquettish, it is better to be obliged to treat a hair twice than to produce an indelible scar.

Now that I have considered the advantages and drawbacks of radiotherapy and electrolysis in hypertrichosis, what advice are we to give to patients who come and consult us? It must be understood that we are not pointing out the indications for the operation itself; for this part of the subject we refer to what we have already said concerning this matter. We must suppose that an intervention is indicated.

When there are only a few hairs, grouped together as in the case of nævi, or scattered here and there in bunches over a large surface, I think that no discussion is possible, and that electrolysis should be advised. This will give the desired result rapidly and certainly. We must never lose sight of the fact that electrolysis is a method of surgical precision, whatever may have been said to the contrary, and with it we do just what we wish and all that we wish. When it is well handled there are but few surprises. But when the case is one of a large hairy nævus, or of an entire beard, the choice between the two methods, the advantages and drawbacks of which we have been discussing, is much more difficult to make. Although very slow in giving a definite result, it would seem that radiotherapy in such cases still requires fewer applications than electrolysis, and is not painful. But with this process there is an uncertainty as to results that makes one cautious. The patient must be fully posted as to the pros and cons, of which

none should be kept back, and should be told of the possibility, rare though real, of cutaneous atrophy with vessel dilatation and even stubborn ulceration.

Electrolysis has in its disfavor its slowless of action, the great number of applications and its consequent demands on the patient's purse. As for the pain, this need not be considered, as the majority of women stand the electric current perfectly well. In short, when the patient has the means, and when the operator is careful and well trained in the treatment, I think that even in such cases as we have just mentioned, electrolysis should be given the preference over radiotherapy. But in actual practice I do not dare to give such advice. I make it an absolute rule to explain to the patients who come and consult me, the present state of the question in full detail,—and then I leave it to them to decide the matter.

# Pathology

## THE RELATION OF INTRACORPUSCULAR CONJUGATION IN THE MALARIAL PLASMODIA TO LATENT AND RECURRENT INFECTIONS

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Introduction. The etiology of latent and recurrent malarial infections has always attracted much attention from the student of malaria and many theories have been brought forward to explain latency and recurrence. It is obvious that the explanation of the one would necessarily explain the other, as the infection must be latent in the system during the periods between recurrence. Almost all of our knowledge of this subject is theoretical and incapable of proof, as one would expect from the difficulties presented in studying it.

It is evident that the plasmodia must exist in some form in the body during the intervals in which no symptoms of malaria are present, and I have already shown, in a previous contribution[1] considering the pathology of latent malarial infection, that plasmodia may be demonstrated in the spleen of patients who have died from some other disease, and in whom no symptoms of malaria were ever present; these plasmodia did not differ in appearance from those observed in the peripheral blood in acute malarial attacks, and, furthermore, were undergoing normal *shizogony* within that organ, but in numbers insufficient to produce clinical symptoms. In such cases it may be urged that after a certain period of multiplication the plasmodia finally become numerous enough to produce symptoms, and thus a relapse follows. While

this is undoubtedly true in some instances, it will hardly account for long interval relapses, for it is impossible to conceive that the plasmodia of malaria can continue to grow and multiply for weeks and months without becoming numerous enough to produce symptoms of the infection.

To overcome this objection, Bignami[2] considers that the plasmodium exists in some latent form, perhaps encapsulated, in the spleen or other internal organ, a form impossible of recognition by our present staining methods, and which, resting as a spore, is only set free under favorable conditions, the nature of which we are ignorant of. Celli,[3] in discussing this subject says: "How are these recurrences explained? It is difficult to say; perhaps they depend on forms resulting from asexual multiplication, that remain inert in some viscera—possibly in the bone marrow—and from time to time, invading anew the blood give rise to new generations of the asexual cycle."

Recently Schaudinn,[4] in an excellent study of *Plasmodium vivax,* states that recurrences are due to parthenogenesis of the *macrogametes* which escape being taken up by the mosquito and remain in the human host; these eventually liberate *merozoites* which penetrate the red blood cell, undergo shizogony, and thus produce a relapse; this process is completed in from 9 to 12 days, and according to Zieman[5] and Mariotti-Bianchi[6] agrees with the period in which relapses most frequently occur.

So far as I know Schaudinn's results have not been confirmed and it is difficult to understand how such a process explains relapses occurring at irregular intervals, as is the case in my experience in the large proportion of recurring cases; in over a hundred cases of malaria in which I could be sure that true relapses occurred, and not reinfections, no marked regularity was present in the development of either the primary or succeeding relapses. One cannot understand how the parthenogenesis of the *macrogametes,* which must occur in a cyclical manner, can be the cause of relapses occurring all the way from 16 to 80 days after the initial attack of fever. For this reason I am inclined to believe, with Bignami and Celli, that the cause of relapse will be found in a resistant form of the plasmodium (a latent form) which is capable of remaining unchanged within the human body for considerable periods of time,

and which, under favorable conditions, undergoes further development and gives rise to the symptoms which are the evidence of a recurrence.

It is this "latent" or "resting" form of the malarial plasmodia that I believe is produced by intracorpuscular conjugation, a form of conjugation occurring within the red blood cells between two young amœbulæ, the morphology of which I have previously described.[7] Ewing[8] was the first American investigator to describe this process, although it had been mentioned by Mannaberg[9] in his writings upon malaria. My conclusions regarding the significance of the process, which are detailed in this paper, are widely different from those of Ewing. He considered the process of rare occurrence and of comparatively little significance. In describing it he says:[10] "In four cases of tertian infection I have encountered appearances which seem to admit of no other explanation than that of conjugation of malarial parasites. In a considerable number of other cases similar appearances were found, but much less frequently. A great many red cells showed double infection with young rings. In many instances these rings were entirely separate, each exhibiting a single large granule of chromatin. Many cells, however, contained two rings which were clearly fused together along one segment of the ring, and two large chromatin granules were then invariably found at different poles of the ring."

Describing what he considers as a later stage of the same process, he says: "On examining the parasites in later stages of development, most of them were found to have lost the ring form, and to have spread out into a large number of threads, with nodal thickenings, variously curled in the red cell. These threads evidently represented the pseudopodia of a very active amœboid stage. The chromatin masses were now subdivided into 10 or 12 granules, but in the majority of the cases the masses were far apart, and showed no tendency to unite. In many cells, however, the amœboid figures were less marked, and the masses of chromatin lay side by side, united by a little achromatic substance."

Regarding the significance of the process Ewing is undecided. He says: "It would seem that a process so fundamental as the conjugation of individuals, if it occurs at all, ought to be an invari-

able feature of every active infection, but there is not sufficient evidence upon which to base any such claim. The four cases referred to as furnishing numerous clear examples of conjugation were selected on account of the abundance of the conjugating forms, but in many other cases less numerous though equally distinct examples were seen, indicating that the process is of very frequent occurrence. On the other hand, it must be admitted that the majority of specimens from routine cases fail to show any distinct traces of the process; from which it may be concluded that conjugation is not an essential feature of the growth of the parasite."

In a later contribution he says:[11] "The extent and significance of this form of conjugation it is difficult to determine. In the cases in which it can be profitably studied, parasites are very abundant, and in most cases few indications of the process can be detected. It is, therefore, probably not essential to sporulation, and when parasites are scanty the chances of finding typical examples of conjugating pairs are greatly reduced, but the peripheral blood may not be a complete index of the process in the internal organs. It seems probable that conjugation occurs in the first generations of the infection, and becomes less frequent as the disease progresses, the infection in the human host thereby tending to limit itself."

The material for my own studies upon this subject consisted in nearly 300 cases of malaria presenting clinical symptoms, observed at the U. S. Army General Hospital at the Presidio of San Francisco, Cal., together with over 100 cases of latent infection observed at the same place, and a series of 75 latent cases in native Philippine children studied at Camp Stotsenburg and 96 cases of acute infection observed at the latter post and in Manila. As a result of my studies, which cover a period of over five years, I am convinced that intracorpuscular conjugation is not an accidental occurrence in the life history of the malarial plasmodia, but is a process which is most essential and one that occurs invariably at a certain time in all acute malarial infections which are uninfluenced by quinine, and also in all recurrent cases in which the infection is of sufficient strength to produce marked clinical symptoms.

Morphology of Intracorpuscular Conjugation.—The process may be roughly divided into three stages:

*First Stage.*—In the first stage or "stage of protoplasmic union," the two young hyalin rings are in contact, and careful examination demonstrates that at the point of contact there is a direct union of the protoplasm; in stained specimens it will be noticed that the chromatin of the nucleus of the two parasites is separate, and that the union begins in the protoplasm of the plasmodia; in fact, it should be stated that intracorpuscular conjugation always occurs between two young hyalin ring forms and is always completed, so far as can be seen, before the formation of pigment. In no case can conjugation be surely recognized after the formation of pigment, and the large pigmented bodies described by Ewing as conjugating bodies in which the chromatin had divided into several distinct masses, are easily recognized as normal presegmenting plasmodia, in which such a division of the chromatin is always present. In this stage the chromatin masses may be situated at any portion of the periphery of the two rings, but very rarely in apposition. I have been unable to detect any differences in the appearance of the two conjugating organisms, for while one may be a little larger than the other, this is not so, as a rule, and the chromatin masses are always of the same size.

*Second Stage.*—In the second stage, which may be designated as that of "complete protoplasmic union," the chromatin masses become situated in the protoplasm of one organism, formed by the gradual union of the protoplasm of the two conjugating bodies; the chromatin granules may be opposite one another or at any portion of the periphery of the plasmodium, sometimes almost in apposition. The complete union of the protoplasm of the two plasmodia results in a more or less ring-shaped organism, slightly larger than either of the original parasites, containing two masses of chromatin, surrounded by achromatic substance.

*Third Stage.*—The third stage of the process, or "stage of chromatic union" is characterized by the union of the two chromatin granules, with the apparent exclusion, in many cases, of a very minute grain of chromatin, before the union is complete.

Briefly stated, then, intracorpuscular conjugation consists in the complete and permanent union of the protoplasm and nucleus

of two young amœbulæ within the red blood corpuscle; I believe it to be absolutely essential to the maintenance of malarial infection in man, and in those instances in which it does not occur the plasmodia undergo asexual sporulation for a limited time and then perish, thus leading to spontaneous recovery; it is present most typically in those cases in which the symptoms are most severe, and is present in all varieties of malarial fever, though most easily observed in the æstivo-autumnal infections.

That the process is observed as often when the non-conjugating plasmodia are in the nearly full grown stage or even in the segmenting stage, as it is when they are in the young hyalin stage, in cases in which there is an infection with only a single group of plasmodia, is conclusive proof to my mind that it is not a mere accidental occurrence or due to amœboid plasmodia; if we add to this that intracorpuscular conjugation occurs always in the same manner and that every stage can be traced in the blood; that the two chromatin granules which are present are invariably of the same size, and that it occurs at definite periods of the malarial infection, I believe that the only conclusion to be reached is that it is a vital process and one that must be of essential importance in the life history of these organisms.

Conjugation in Protozoa in General and its Significance.—In order to understand the significance of intracorpuscular conjugation in the malarial plasmodia it is necessary to review briefly the phenomena and significance of conjugation as it occurs in other protozoan organisms, for it is only by thus summing up, as it were, the significance of the process in all forms of the protozoa in which it occurs, that we are enabled to arrive at any conclusions regarding its significance in the plasmodia of malaria.

The process of conjugation is common among the Protozoa and may be observed in all its gradations from the union of absolutely similar organisms, in which sex cannot be differentiated, to the union of highly specialized forms in which the male and female organisms can be easily distinguished.

The Rhizopoda.—Conjugation has been observed but rarely among the Rhizopoda, most frequently among the *Amœbina* and *Heliozoa*.

Among the *Amœbina* conjugation is probably much more common than is generally supposed. Holman[12] observed the temporary union of a large and small amœba, which resulted apparently in the production of swarm-spores in each. Penard[13] describes the permanent union of different sized individuals in *Amœba spatula,* the larger absorbing the smaller. I have observed conjugation in *Entamœba coli* several times, the process consisting in the permanent fusion of apparently similar organisms, the protoplasm of the two blending, followed by the fusion of the nuclei; in *Entamœba dysenteriæ* (*histalytica*) I have observed conjugation frequently, but only when the surroundings were abnormal, as in cold fæces, etc., I believe that the process is of greater import in the life history of these parasites than is generally thought.

Among the *Heliozoa* conjugation has been certainly demonstrated in *Actinophrys sol* and in *Actinosphœrium eichornii* by Schaudinn,[14] in the former, free swimming forms unite, coalesce, and develop a firm protective covering; the union is protoplasmic, the nuclei remaining distinct; the latter finally divide, thus making four nuclei; two of these fuse and give rise by mitosis to daughter-cysts, while the remaining two degenerate and disappear. In *Actinosphœrium eichornii* conjugation is stated to be common before reproduction commences.

The Flagellata.—Among the Flagellata conjugation is very common and may occur between similar individuals, or between individuals dissimilar in appearance, that is, it may be asexual or sexual in character. The product of the conjugation or *zygote* gives birth to the motile organisms which reproduce without conjugating. To Dallinger and Drysdale[15] we are indebted for much of our knowledge regarding conjugation among the monads.

In *Monas dallingeri* (*Cercomonas crassicauda*) reproduction occurs by fission of the free swimming forms and by the conjugation of amœba-like forms, which upon coming in contact immediately coalesce; this "resting stage" persists for about six hours, when the organism ruptures and liberates multitudes of minute spores, which develop into the adult organism and reproduce by fission as before. In *Oikomonas dallingeri* certain of the organisms do not proceed to fission but undergo changes in morphology consisting in the withdrawal of the flagella and great increase in the

size of the nucleus; these bodies coming in contact with ordinary adult individuals, fuse with them, and become encysted; after from four to five hours the cyst ruptures and very minute spores are liberated which develop into the ordinary dividing forms. In *Heteromita uncinata* the conjugating organisms are differentiated by their size, larger and smaller individuals being seen, the former possessing a contractile vacuole at the anterior end; conjugation consists in the absorption of the smaller form by the larger, followed by encystment and finally by the rupture of the cyst and the liberation of spores which become the ordinary dividing forms.

I have repeatedly seen undoubted conjugating forms in *Trichomonas* and *Cercomonas intestinalis* as well as in *Lamblia intestinalis.* In these species conjugation was preceded by the withdrawal or loss of the flagella and the development of irregular or round amœba-like forms; contact of two such organisms resulted in complete fusion and the production of a cyst-like body which appeared clear and hyalin. I have not been so fortunate as to observe the rupture of the cyst and the liberation of the young spores.

Pringsheim[16] describes the process of conjugation in *Pandorina* as occurring between two individuals of the swarm-spore, which meet and fuse; the resulting organism encysts and develops within the cyst a swarm-spore which is liberated when the cyst is placed in a favorable environment; the liberated swarm-spores divide and eventually form the sixteen celled *Pandorina* colony.

Among the *Hæmoflagellates* conjugation has been observed in *Trypanosoma lewisi, Trypan-osoma equinum* and *Trypanosoma equiperdum;* the phenomena of conjugation in *Trypanosoma lewisi* will be spoken of later.

The Sporozoa.—Among the Sporozoa the process of conjugation is highly developed and becomes largely a sexual phenomenon, the male and female organisms being, in most instances, easily distinguishable. However, conjugation in this class of organisms may be very simple as has been already shown in the description of intracorpuscular conjugation in the malarial plasmodia, where no sex differentiation can be demonstrated.

In the *Gregarinida, Coccidiida,* and *Hæmosporidia* conjugation occurs and has been studied by Schaudinn and Siedlecki,[17]

Wolters,[18] Grassi and Feletti,[19] Celli and Sanfelice,[20] MacCallum[21] and Ross.[22]

In the *Gregarinida,* sporulation is generally preceded by the fission of two gregarines and their encystment. Wolters[23] in *Monocystis agilis* describes the process of conjugation as consisting of the following phenomena: apposition of the end of each organism; mitosis of each nucleus, one portion of each being extruded, the other two daughter-nuclei fusing through an opening in the wall of the organisms at the point of apposition; mitosis of the fused nucleus, one daughter-nucleus then going to each conjugant; mitosis of each daughter-nucleus and the formation of spores. This method of conjugation has not been confirmed.

In those instances in which two gregarines unite and become encysted each nucleus reduces, a large portion of it disappears, and as shown by Siedlecki,[24] a new nucleus is formed which divides by mitosis; the daughter-nuclei now divide and the division is repeated until the cyst is filled with nuclei. Each nucleus is surrounded by a portion of the protoplasm and thus *gametes* are formed which fuse and produce the *sporozoites* or the infecting organism. It will be observed that in this case two forms of conjugation occur, one when the two gregarines unite and one when the *gametes* fuse within the cyst produced by the first form.

Coccidiida.—Shuberg[25] was the first to suggest conjugation in the *Coccidiida* and Schaudinn and Siedlecki the first to demonstrate that this process is a developmental necessity in these organisms, that it is a true sexual phenomenon, and results in the fertilization of the female organism. In this class of organisms sexual dimorphism exists, and an alteration of generations occurs, one asexual and the other sexual; in the asexual cycle the coccidia are intracellular in the host, where they sporulate and the *merozoites,* leaving the host cells, invade new ones; in the sexual cycle conjugation occurs between specialized organisms, the male or *microgamete* and the female or *macrogamete* and *sporogony* follows. Conjugation occurs within the infected individual but is extracellular.

*Hæmosporidia.*—It is now well known that sexual conjugation occurs among the *Hæmosporidia* of both animals and man. The plasmodia of malaria, for example, undergo a sexual cycle of

development in the body of the mosquito and an asexual cycle in the blood of man. In the former, conjugation is absolutely essential to sporulation, but here, in contradistinction to the intracorpuscular form of conjugation which occurs in the blood of man, the conjugating organisms are sexually differentiated, and in addition, intracorpuscular conjugation is not essential to sporulation, but only to the continuation of the infection; in the mosquito conjugation is a fertilizing process *per se,* while intracorpuscular conjugation simply stimulates the organism to renewed activity; the first is a true sexual process, the latter an asexual one, and thus in the human and mosquito cycles of the malarial plasmodia conjugation is illustrated in its simplest and most highly developed phases.

In *Lankestrella* and *Karyolysus,* hæmosporidian forms inhabiting cold blooded vertebrates, Labbe[26] has described a process of conjugation which approaches very closely to intracorpuscular conjugation in the malarial plasmodia. A *trophozoite,* after developing for a while in a blood corpuscle, becomes free and conjugates with a similar form; the *zygote* thus produced may penetrate a second blood corpuscle or may invade a cell of the spleen, kidney, or bone-marrow, where it becomes encysted; in the cyst are developed *sporozoites* which are liberated when conditions are favorable.

In *Halteridium,* MacCallum[27] demonstrated the occurrence of sexual conjugation and thus led the way to our present knowledge of the similar process in the life cycle of the malarial plasmodia within the mosquito.

The Infusoria.—It was in this class of the Protozoa that conjugation was first correctly interpreted by Bütschli [28] and Englemann,[29] and here it occurs almost universally. In no other class of the protozoa is the truth of the statement that the process is one of " rejuvenation " so well illustrated. Reproduction normally occurs in this class by binary division, or less often, by multiple division after encystment; whatever the method, reproductive activity finally ceases and conjugation then occurs, restoring the vital activities of the cells by bringing about a regeneration of the protoplasm and especially, of the nucleus. Maupas [30] and Hertwig[31] have demonstrated that when conjugation occurs, definite

nuclear changes take place, consisting in nuclear reduction, fusion, division and the formation of a new macro-nucleus. The union may be temporary or permanent.

In *Paramecium aurelia,* Balbiani[32] demonstrated that conjugation occurred after a series of generations had been evolved by ordinary transverse division, and that it lasted for five or six days, during which time important changes occurred within the conjugants, which finally separated and gave rise to individuals capable of developing as usual.

Wising,[33] Woit,[34] Gourvitch,[35] and Strong,[36] have stated that the conjugating pairs unite and form oval cysts, but their work has not been confirmed and it is probable that the process described by Strong, i.e., the simple fusion of adult organisms is what really occurs. In all probability, after a certain period of time, the conjugants separate and become reproductive as before.

General Significance of the Process of Conjugation in the Protozoa.—The process of conjugation in the Protozoa was first observed and described by O. F. Muller.[37] His work was confirmed by Balbiani,[38] who claimed that certain of the Protozoa not only reproduced by simple division but also by conjugation, the latter being a sexual act leading to the formation of young parasites. It is to Bütschli [39] that we owe the correct interpretation of conjugation in the Protozoa. He observed that continued reproduction of many of these organisms by simple division led eventually to the exhaustion of the capability of the division, and thus to the death of the organisms. He, therefore, regarded the process of conjugation as one intended to bring about rejuvenescence of the nearly exhausted individuals of a generation of organisms. Englemann [40] confirmed this interpretation of conjugation, and thus defines the process: "The conjugation of the infusoria does not lead to reproduction through 'eggs,' 'embryonic spores,' or any other kind of germ, but to a peculiar developmental process in the conjugating individual, which may be designated as reorganization." In other words, conjugation is intended to bring about a restoration to former reproductive activity, this result being secured by a rejuvenescence of the vital activities of the organism.

Calkins,[41] to whose admirable work I am indebted for many of the references in this contribution, in his discussion of the subject says: "If, as Minot suggested, every newly-born organism be regarded as having a certain initial potential energy which is gradually used up in its life activities to be restored by conjugation, then the union of two cells may be interpreted as a renewal of vigor or a rejuvenescence. The force of these views as to the need of conjugation for different species of infusoria, at least, can hardly be questioned, for, as repeatedly stated in the previous chapters, reproduction by simple division may go on for a certain number of generations, but cannot continue indefinitely, unless at certain intervals, which Maupas has shown to be more or less definite, two individuals unite in conjugation. This union, in some wholly unexplained way, imparts to each of the conjugants a renewed vitality, or in Bütschli's words, a renewal of youth, expressed by increased activity in movements and reproduction. Conjugation thus, as R. Hertwig insists, is not the beginning of a series of reproductive acts but occurs at or near the end of such a series. The phenomena of the so-called sexual reproduction and sex differentiation have, in all probability, grown out of this apparently fundamental requirement of living protoplasm, namely, the periodic union of two cells."

That conjugation is not a reproductive act in many of the Protozoa is shown by the fact that the time consumed in the process is sufficient for reproduction by simple division to occur many times; this is well illustrated in those Protozoa in which a resting stage succeeds conjugation.

While fertilization is generally the result of conjugation it does not follow that the act is a reproductive one, for, as has been pointed out by Hertwig;[42] "A reproductive process is bound up with the encystment of *Actinosphærium,* whereby a mother-cyst gives rise to many primary cysts, each primary cyst to a germ-sphere, each germ-sphere to new individuals. Reproduction here precedes fertilization and the latter has no effect upon the former."

In reviewing the phenomena of conjugation in the Protozoa it has been shown that in many of them, after the union of the conjugants, a "resting" or zygote stage succeeded. In this stage the organisms invariably possess greater resistance to injurious influ-

ences, and may remain latent, so to speak, no further development occurring until conditions are favorable for ordinary growth and reproduction. This is also true in all those lowly forms of plant life in which conjugation has been observed as well as in many of the Protozoa. A most typical example is found in *Panderina morum,* in which the *gametes* conjugate and assume a "resting" form, which is encysted; under favorable conditions the cyst ruptures and one or more individuals emerge, and dividing, in time the typical colony is again formed.

The conjugation of a protozoan organism within the body of its intermediate host is purely sexual in its nature and is followed at once by reproduction; such a type of conjugation should be clearly distinguished from that in which there is union of two individuals, similar in appearance, followed by a period of inactivity or a zygote stage. The sexual type, occurring within an intermediate host, is well illustrated by the union of the *macrogametes* and the *microgametes* of the malarial plasmodia within the mosquito, while intracorpuscular conjugation of the same organisms is a typical example of asexual conjugation. It is apparent, therefore, that asexual conjugation is not a reproductive act but one intended to preserve the function of reproduction in a race threatened with extinction by repeated division, or, perhaps, intended to evolve a resistant form when conditions are unfavorable for reproduction in the ordinary way. Again to quote Calkins:[43] "From all the facts shown at the present time, the only conclusion that can be drawn is that conjugation, apparently, is not the cause of reproduction, but as Bütschli, Englemann, and Minot long since pointed out, in some unknown way provides the energy for continuing the functions of the individual, including the power of reproducing."

Significance of Intracorpuscular Conjugation and its Relation to Latent and Recurrent Malarial Infections.—Having thus briefly reviewed the process of conjugation and its significance as it occurs in the Protozoa in general, we are in a position to consider the significance of that peculiar form of conjugation in the malarial plasmodia which I have termed intracorpuscular conjugation. The conjugation of malarial plasmodia within the red blood corpuscle is asexual, it being impossible to

detect any constant difference in the appearance of the two conjugants. It occurs between two young, unpigmented amœbulæ, and is completed, so far as can be seen, by the permanent union of both nucleus and protoplasm; the process may be observed in all acute infections uninfluenced by quinine and in recurrent infections, but only in latent infections, in the peripheral blood, just before the appearance of clinical symptoms.

Continued study of this subject has confirmed my belief that the process is intended to maintain the malarial infection in the blood of man, and that it occurs whenever the race of plasmodia are in danger of dying out from repeated sporulation in the usual manner; it is therefore most frequently observed in the latter part of an acute attack, instead of before the appearance of clinical symptoms. I am also convinced that in this process there lies, in all probability, the explanation of latent and recurrent malarial infections.

It has been shown, by many observers, that conjugation occurs in many, if not in most all, organisms when unfavorable developmental conditions arise, such as exhaustion from repeated division, insufficient nutriment or the presence of conditions in the environment that are unfavorable to growth in the usual manner; it has also been shown that under such conditions a "resting" or zygote stage succeeds conjugation, in which the usual vital activities of the organism are wholly or in part suspended until the conditions again become favorable, when the vital activities are resumed and reproduction occurs as before.

If we consider carefully the phenomena of intracorpuscular conjugation as seen in the malarial plasmodia, it is evident that they conform to those observed during conjugation in many of the Protozoa, and that, if there is any value in analogy, the conditions leading to the process, and its significance, are similar. Considered in this way I believe that intracorpuscular conjugation can be explained, and that the theory of the ætiology of latency and recurrence in malaria which follows is one that is worthy of careful study and one that is well supported by the known significance of conjugation in other Protozoan organisms.

Intracorpuscular conjugation in malaria occurs after a series of reproductions by spore formation, during which time the initial

potential energy of the race of plasmodia has gradually decreased; during this same period the clinical symptoms of malaria have been present, and the environment of the plasmodia rendered unfavorable by the administration of drugs such as quinine, or the elaboration of antitoxic materials by the cells of the invaded individual; as a consequence, decreased ability to reproduce by spore formation leads to intracorpuscular conjugation, and the formation, thus, of a resistant form of the plasmodium. The conjugation occurs within the red blood cell because only here can nutriment be obtained for further development.

When conjugation is completed by the union of the protoplasm and nucleus of the two conjugants, growth occurs at the expense of the red cell, until finally the entire cell is destroyed, and the round, pigmented organism is liberated; this form now probably becomes encysted, and enters upon a "resting" or zygote stage, and it is my belief that it is this stage that has been considered by Schaudinn[44] as a *macrogamete,* which by parthenogenesis, gives rise to recurrences.

This stage is probably more resistant to injurious influences, such as quinine, than other forms of the plasmodium, and may continue unharmed in one of the internal organs, as in the spleen, or, more probably, the bone marrow, for long periods of time; when conditions are favorable the cyst ruptures and liberates a generation of spores which have meanwhile developed within it; these young plasmodia penetrate the red blood corpuscles and reproduce, as is usual, by spore formation. Latency is thus rendered possible by the resistance of the "resting" or zygote stage, and recurrences are due to the liberation and subsequent sporulation of the young plasmodia.

In cases in which this form of conjugation is present, numerous large pigmented plasmodia are present, both within and without the red cells, which show no evidence at any time of segmentation or flagellation; in these the pigment is small in amount, and distributed irregularly in very fine granules; a double outline is often observed and in æstivo-autumnal infections no difficulty is found in distinguishing them from the round or oval bodies resulting from the development of the crescents; they are often very numerous in the blood of cases in which intracorpuscular conjuga-

tion is present, and, so far as my experience goes, they do not occur in cases in which this process is absent; in æstivo-autumnal infections these bodies are only seen in blood obtained by splenic puncture.

These bodies are probably the ones concerned in the production of the latent forms and eventually all become encysted and situated in some internal organ or in the bone marrow; Ewing[45] describes similar bodies in the bone-marrow of a case of fatal pernicious malaria due to the æstivo-autumnal plasmodia.

It would seem that the growth of the conjugating form within the red cell is rapid until the destruction of the cell, when the plasmodium is liberated and enters upon the "resting" or zygote stage; the duration of this stage probably varies with conditions, but I believe that it lasts for several days at least, even in the most favorable environment. Reasoning from analogy, this stage must continue for some time, for, as has been shown for the Protozoa, by Bütschli,[46] Maupas,[47] and Hertwig,[48] the two conjugating individuals might by simple division give rise to many others during the time occupied in conjugation, and this is true of every organism in which asexual conjugation occurs, so far as I know; it would indeed be strange if the malarial plasmodia were exceptions to so general a rule, and therefore it follows that the "resting" or zygote stage must continue for several days, and that intracorpuscular conjugation, admitting that it produces this form of the plasmodia, is the cause of latency and recurrences. The periods of time between relapses, which vary somewhat, but are remarkably uniform when quinine has not been administered, are explained by the time consumed in the completion of the process of intracorpuscular conjugation and the development of the young plasmodia within the *zygote,* while the marked irregularity in the period between relapses after quinine has been administered is explained by the liberation of the young plasmodia only when the environment is favorable, *i.e.,* when the quinine has been discontinued or the amount given greatly reduced. We thus see relapses quickly follow the discontinuance of quinine or the reduction of the dose, and Celli,[49] in his suggestion that relapses may depend upon asexual forms which remain inert in some viscera, gave in all probability the true explanation of recurrences in

malaria, inert asexual bodies of Celli, being the *zygote* or "resting" form of plasmodia, produced by intracorpuscular conjugation. That such a latent or "resting" form of the parasites of malaria is present somewhere in the body in malarial infection is proven by the fact that the withdrawal of quinine from persons who have been taking it for weeks, is often followed by a relapse and the reappearance of the plasmodia in the blood. It is impossible, without producing symptoms, to believe that *shizogony* has occurred in such cases for weeks even when quinine has been administered in large doses; and while, as I have shown, in latent cases *shizogony* does occur within the spleen without symptoms being produced, it should be remembered that in the cases in which this was observed, no quinine was being administered, and symptoms would probably have soon appeared had the patients lived.

As has been pointed out, two types of conjugation are present in the complete life history of the malarial plasmodia: one, asexual, occurring within the red blood corpuscles of man; the other, sexual, occurring within the mosquito. The question arises: Do two similar types of conjugation occur in any other Protozoan organism?

It should be remembered that the list of the Protozoa in which the life cycle has been followed through an intermediate host is not very large, and, therefore, our knowledge of the exact details of asexual and sexual conjugation in any single organism, at all stages of its development, is very limited. Among the *Hæmoflagellates,* however, recent research has confirmed the presence of asexual and sexual conjugation in the life cycle of *Trypanosoma lewisi;* asexual conjugation, occurring in the blood of the rat, has been studied, in this organism, by Bradford and Plimmer,[50] Doflein,[51] and Stassano;[52] and the researches of Prowazek[53] prove that sexual conjugation occurs in an intermediate host. This observer found that *Trypanosoma lewisi* undergoes a portion of its life cycle within the rat louse, *Hæmotopinus spinulosum;* after reaching the mid gut of the louse, reduction of the nucleus occurs, and male and female *gametocytes* are produced, which are easily distinguished; sexual conjugation between these forms follows, the *zygote* becomes an *ookinete,* and this eventually results in a single trypanosome, which again infects the rat and reproduces as usual.

From the researches of the investigators named it is evident that in *Trypanosoma lewisi* asexual conjugation occurs in the blood of the rat and sexual conjugation in the mid-gut of the rat louse, and it is probable that further research will demonstrate that asexual conjugation is of constant occurrence in those Protozoa which require an intermediate host for the completion of their life cycle, sexual conjugation occurring within the intermediate host, asexual conjugation within the definitive host.

From my studies of the subject I believe that the following conclusions are justified regarding the significance of intracorpuscular conjugation in the malarial plasmodia:

1. Intracorpuscular conjugation is the principle cause of the maintenance of malarial infection in man, and its absence the cause of spontaneous recovery.

2. It maintains malarial infection by producing a "resting" or zygote stage of the plasmodia, which is resistant to quinine and other injurious influences.

3. It is the cause of latent and recurrent malarial infections, the zygote stage remaining dormant or "latent" until conditions are favorable, when it gives birth to several young plasmodia, which penetrating the red blood corpuscles, by their growth and sporulation, cause a recurrence of the infection.

These conclusions are justified by the following:

1. The presence of the process in all acute and recurrent infections, and its absence in cases which recover spontaneously.

2. The fact that during the time consumed in conjugation, if asexual, in all other Protozoa, many generations of the organism could have been produced by division or sporulation in the usual manner.

3. The fact that such a "resting" or zygote stage must exist, as proven by the recurrence of malarial infections after the discontinuance of quinine which has been given for long periods of time.

4. The fact that in cases which have been treated at once with sufficient doses of quinine and for a sufficiently long period, intracorpuscular conjugation is never seen, and that in such cases, relapses are very rare, if they ever occur.

5. The presence of numerous large pigmented bodies in the blood in cases in which the process is most marked, both intra- and extra-cellular, and which, so far as my experience goes, are not seen in cases in which the process is absent.

6. The "argument from analogy" which indicates that the significance of the process of asexual or intracorpuscular conjugation in the malarial plasmodia is similar to that of the same process in other of the Protozoa.

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# INDEX TO VOLUME III

## (SEVENTEENTH SERIES)


### A

Abdomen, enlargement of, 104
Abscess of liver, 153
Adiastematia, early, 213
late, 213
Age and bloodpressure, 64
Albuminuria, pathologic non-renal, 98
physiologic, 97
renal, 99
significance of, 96
Alcohol and bloodpressure, 67
Alcoholic multiple neuritis, 253
Ancel and Bouin, Spermatic insufficiency and diastematic insufficiency, 211
Aneurism, surgical treatment of, 137
Arsenical multiple neuritis, 253
Atopomenorrhœa, 179

### B

Beal, Raymond, How to turn back the upper lid, 246
Birth injuries of eye, 217
Bloodpressure and nephritis, 69
in infectious diseases, 62
in tuberculosis, 61
method of determination of, 62
Bloodvessels, anastomosis of, 140
surgery of, 131
suture of, 139
Bouin and Ancel, Spermatic insufficiency and diastematic insufficiency, 211
Bownaire, E., Collargol in puerperal infection, 170
Brocq, L., Present treatment of hypertrichosis, 262
Bronchopneumonia, metallic ferments in, 36
Brown, Mark A., General abdominal enlargement, with special reference to the hepatic cirrhoses, 104
Buchanan, Leslie, and Thomson, Ernest, A contribution to the study of ocular birth injury, 217
Bullock, E. S., Curability of tuberculosis, 51

### C

Cancer, endemic occurrence of, 114
Carbohydrates and diet, 19
Carcinoma of choroid, 77
of liver, primary, 75
Carcinomatosis, 82
Casts, significance of urinary, 100
Cataract, extraction of, in capsule, 234
Choroid, carcinoma of, 77
Cholangitis, 154
Cholecystitis, 149
Cholecystostomy, 150
Cholemia, 155
Cirrhosis of liver, 104
pathology of, 111
Coccidia, conjugation in, 281
Collargol in puerperal infection, 170
Conjugation in protozoa in general, and its significance, 278
morphology of intracapsular, 277
Corneal opacities, 221
Craig, Charles F., The relation of intracapsular conjugation in the malarial plasmodia to latent and recurrent infections, 273

### D

Depilatory preparations in hypertrichosis, 266
Diastematic insufficiency, 211, 214
temporary, 215
Diet in acute gastritis, 95

Dietetics, practical and theoretical considerations concerning, 1
Diets, caloric value of liquid, 10
Digestive disorders and massage, 46

E

Ecchymosis of eyelids, 217
Edsall, David E., Some practical and theoretical considerations concerning dietetics, 1
Electrolysis in hypertrichosis, 267
Endemicity of cancer, 114
Eye, birth injuries of, 217
Eyelid, how to turn back upper, 246
Eyelids, ecchymosis of, 217

F

Fats and diet, 19
Ferments in pneumonia, metallic, 25
Flagellata, conjugation in, 279
Fluids and diet, 21
Foot, perforating ulcer of, 159
Fractures and massage, 46
Friction massage, 40

G

Gallbladder and gallducts, causes of inflammation of, 149
  inflammation of, 149
  catarrhal inflamation of, 150
  empyema of, 150
  gangrene of, 150
  perforation of, in typhoid fever, 152
Gastritis, acute, 89
  causes of acute, 91
    diet of acute, 95
  in infants, 92
  pathology of acute, 93
  symptoms of acute, 93
  treatment of acute, 94
Gay, Frederick P., The etiology and experimental study of syphilis, 199
Gonorrhœa and bloodpressure, 68
Green, F. K., and Hunter, Q. W., Atopomenorrhœa, 179

H

Hair, eradication of, 266
Hall, Arthur J., Perforating ulcer of the foot, its etiology and treatment, 159
Hæmorrhage and bloodpressure, 72
Hæmosporidia, conjugation in, 281
Heredity and cancer, 118
Hipjoint disease, 167
Hunter, Q. W., and Green, F. K., Atopomenorrhœa, 179
Hydrogen peroxide in hypertrichosis, 279
Hypertrichosis, present treatment of, 262
Hysteria and massage, 46

I

Immunity in cancer, 126
Infection and cancer, 115
Inflammation of gallbladder and gallducts, 149
Infusoria, conjugation in, 282
Inoculability of tumors, 120

K

Kidney, factors in the estimation of diseases of the, 96
  function of, 102
Kneading massage, 40

L

Lenscapsule, rupture of, 243
Liver, abscess of, 153
  cirrhosis of, 104
  primary carcinoma of, 75
Locomotor ataxia and massage, 46
Loeb, Leo, Observations on the inoculability of tumors and on the endemic occurrence of cancer, 114
Lymphadenitis, tuberculous, 165

M

Malaria, latent and recurrent, 273
Malarial plasmodia, relation of intracorpuscular conjugation in, to latent and recurrent infections, 273
Massage, 40
  effects of, 43
  indications of, 44
  in whooping-cough, 45

Matas operation for aneurism, 138
Mechanotherapy, 39
Menstruation, vicarious, 179
Metallic ferments in pneumonia, 25

N

Nephritis and bloodpressure, 69
eyegrounds in, 70
Nerve disorders and massage, 46
Neuralgia and massage, 46
Neurasthenia and massage, 46
Neuromyositis, 253

O

Obesity and massage, 46
Ocular muscles, paralysis of, 226
Orbital birth injuries, 226
Osteomyelitis, tuberculous, 166

P

Palladium hydrasol in pneumonia, 31
Percussion in massage, 41
Perineal prostatectomy, 191
Plasmodium malariæ, conjugation in, 273. 287
Pneumonia and bloodpressure, 68
fibrinous, 75
treatment of, 25
Polyneuritis, dietetic, 261
due to unusual causes, 253
infectious, 260
Porter, William Henry, Two cases of primary carcinoma of the liver: one with fibrinous pneumonia; one diagnosticated by paracentesis abdominis, 75
Predigestion of foods, 22
Pressure in massage, 41
Prostatectomy, perineal, 191
Prostatitis, conservative perineal prostatectomy for chronic, 191
Protozoa, conjugation in, 283
Puerperal infection, collargol in, 170
Pulserate and bloodpressure, 67

R

Retina, hæmorrhage from, 218
Rheumatism and massage, 46
Rhizopoda, conjugation in, 278
Rickets, 219
Roberts, John B., Some surgical aspects of tuberculosis, 162
Robin, Albert, On the treatment of pneumonia, and especially the action of metallic ferments in this disorder, 25
Roentgen rays in hypertrichosis, 263

S

Serum to immunize against cancer, 128
Sex and bloodpressure, 63
Shaving in hypertrichosis, 266
Skin diseases and massage, 47
Sommerville, David, Acute gastritis, 89
Spermatic insufficiency, 211
Spirocheta pallida, 202
Sporozoa, conjugation in, 280
Sprain and massage, 46
Stanton, William B., The bloodpressure in tuberculosis, 61
Stretching in massage, 41
Stroking in massage 42
Swedish movements, 45
Sweet, J. E., The surgery of the bloodvessels, 131
Syphilis and bloodpressure, 68
etiology and experimental study of, 199
vaccination treatment of, 206

T

Talma's operation for cirrhosis of the liver, 110
Testicles, insufficiency of, 211
Thomson, Ernest, and Buchanan, Leslie, A contribution to the study of ocular birth injury, 217
Time of day and bloodpressure, 63
Transfusion, history of, 131
method of, 132
Tuberculin, 59
test, 60
Tuberculosis, autoinfection with, 164
bloodpressure in, 61, 67, 69
curability of, 51
advanced, 58
incipient, 58
early diagnosis of, 59
polyneuritis due to, 254
routes of infection with, 163
surgical aspects of, 162

Tuberculous lymphadenitis, 165
osteo-myelitis, 166
spondylitis, 167
Tumors, inoculability of, 114
Typhoid fever, bloodpressure in, 68
perforation of gallbladder in, 152

U

Ulcer of foot, perforating, 159
Urea and uric acid secretion in pneumonia, 26

V

Vaccination treatment of syphilis, 207
Vaughan, George Tully, Inflammation of the gallbladder and gallducts, 149
Vertebral column, tuberculosis of, 167
Vibration massage, 41, 48
Vicarious menstruation, 179
Vitreous, escape of, 242

W

Wainwright, John W., Mechanotherapy, 39
Wallace, Raymond, The salient factors in the estimation of renal disease, 96
Weber, F. Parkes, Some cases of polyneuritis (including neuromyositis) apparently not due to alcohol, arsenic or any of the ordinarily recognized causes, 253
Weight and diet, 6
Whooping-cough, massage in, 45
Williamson, J. Rutter, Extraction of cataract in the capsule, 234

Y

Young, Hugh H., Operation: conservative perineal prostatectomy for chronic prostatitis, 191

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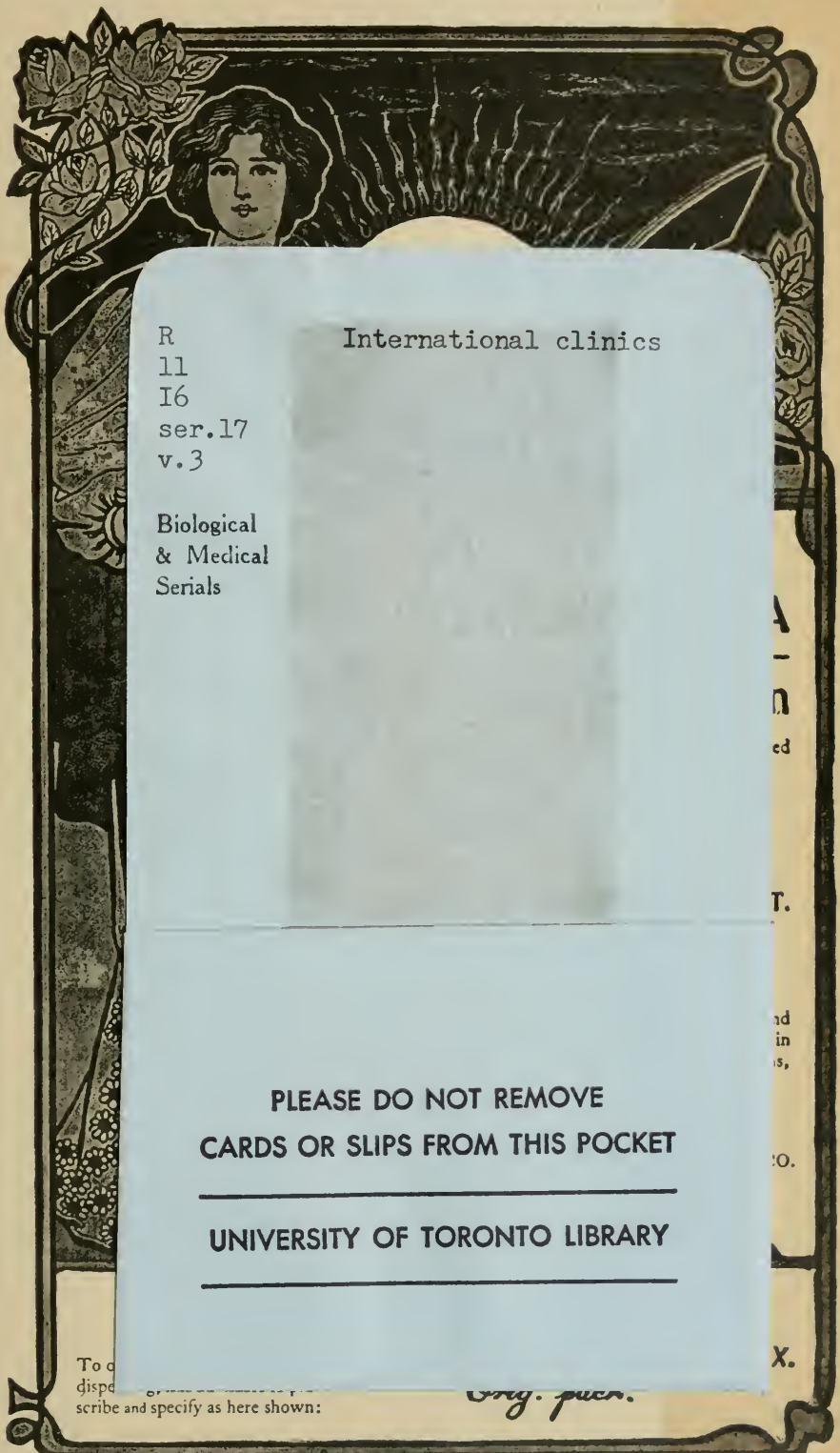

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